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SURFACTANT INTERACTION AND PERSISTENCE AT THE CONTACT LENS SURFACE

by

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Doctor of Philosophy

ASTON UNIVERSITY

March 2014

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Thesis Summary

ASTON UNIVERSITY

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SARAH MARIA CARNELL

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of Doctor of Philosophy

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The interaction of poloxamer and poloxamine (Pluronic® and Tetronic®) surfactants with hydrogel and silicone hydrogel contact lens surfaces is of interest for this thesis. The persistence of surfactant molecules at the lens surface can indicate how long the surface has been modified. It is therefore important to observe and characterise the surface and surfactant behaviour separately.

Characterisation of the contact lenses was carried out through dehydrated sessile drop measurements and surface energy calculations. Silicone-containing materials tended to be most hydrophobic regardless of water content.

Static and dynamic surface tension measurements were used to assess the surfactants and the critical micelle concentration was also observed. Pluronics® and Tetronics® do not behave as simple low molecular weight surfactants; their structure and size mean they are less mobile in solution and may be able to form mono molecular micelles. Surfactants with different molecular structure, molecular weight and hydrophobicity were used to observe how these properties affect surface tension behaviour and influence surfactant persistence.

The aim of the work was observe the persistence of surfactants at the lens surface, any difference between the surfactant persistence, and the possibility to predict surfactant persistence on a lens. The ex vivo work presented here shows little distinction between surface tension measurements over time or between treated and untreated materials. It is not possible to measure in vivo surfactant persistence with surface tension techniques and therefore necessary to create in vitro models to assess surfactant behaviour. A simplified in vitro eye model was created to assess preliminary observations. These results and observations were used to progressively alter the model and create a more 'eye-like' system.

Large hydrophobic Tetronics® were most persistent at the lens surface; hydrophobic drive was considered the most influential factor. In addition to this, the contact lens material and condition prior to surfactant treatment also had an effect on persistence. Materials containing PVP showed increased surfactant persistence, which was increased further when the lenses were dehydrated prior to surfactant treatment. Lens dehydration had no effect on persistence if PVP was not present in the lens material.

Keywords: Contact Lenses, Surface Modification, Silicone Hydrogels, Tetronics®, Surface Tension

For my family

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Abbreviations

ADC	Dailies All Day Comfort
BL	Boundary Layer
CMC	Critical Micelle Concentration
COF	Coefficient of Friction
CP	Copolymer
EWC	Equilibrium Water Content
HD	Hydrodynamic Lubrication
HEMA	Hydroxyethyl methacrylate
HPLC	High-Performance liquid chromatography
HPMC	Hydroxypropyl methylcellulose
MA	Methacrylic acid
ML	Mixed Lubrication
MPS	Multi-Purpose Solution
PEG	Polyethylene glycol
PEO	Polyethylene oxide
PET	Polyethylens terephthalate
PMMA	Polymethyl methacrylate
PPO	Poly propylene oxide
PTFE	Polytetrafluoroethylene
PVP	Polyvinylpyrrolidone
SFE	Surface Free Energy
SS	Stick-Slip
ST	Surface Tension
TRIS	Trimethyl siloxysilyl
F127	Pluronic® F127*
904	Tetronic® 904*

* Please see Figure 2.1.3.1 for further explanations.

Chapter One

Introduction

'We live, I regret to say, in an age of surfaces.'
Lady Bracknell, The importance of being Earnest: Act III

1. Introduction

This thesis is concerned with the selective adsorption and retention of surfactants at hydrogel/polymer surfaces, but more specifically with the adsorption and retention of surfactants that are used in multi-purpose care solutions (MPS) at the surface of hydrogel contact lenses.

This introductory chapter is therefore concerned with the nature of surfactants, their surface tension and related phenomena such as critical micelle concentration (CMC). It is also concerned with contact lenses, in particular the nature of their surfaces and the methods for defining this.

The main thrust of the thesis thereafter involves the study of surfactants, their interaction with contact lens surfaces and the development of an in vitro system to mimic aspects of in-eye behaviour.

‘Contact lenses are optical devices’ [1]. They are clear discs that are placed directly onto the cornea and are largely used to correct vision. The contact lens is a foreign object in the eye and causes the natural system to behave differently to compensate. The most common reason for discontinued use of contact lenses is wearer discomfort[2].

Contact lens companies endeavour to improve comfort. Over the years this has been addressed in several ways, including increasing the water content to reduce modulus, plasma coating the lens surface and internal or external wetting agents. The majority of lens modifications to improve comfort are surface-related and involve increasing the wettability, which has been frequently linked to increased comfort [3-6] (it is not the only factor).

The work presented in this thesis is directed towards the understanding of the interaction between contact lens materials and contact lens cleaning solutions in the ocular environment. There are many different contact lens materials, of which this thesis deals with conventional hydrogels and silicone hydrogels. They all have different bulk and surface properties that are designed to be comfortable, safe and correct vision.

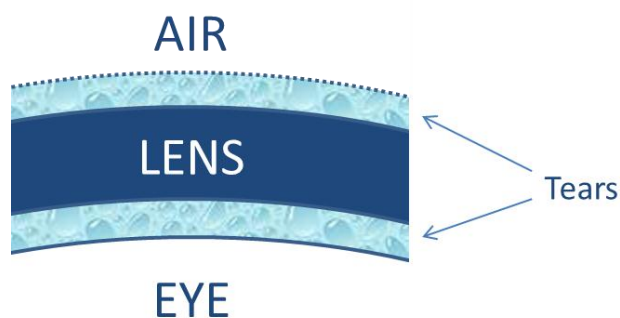


Figure 1.1 The tear/contact lens interface

The interfaces considered here are not only that between the lens and tears (see Figure 1.1) but also the additional solutions that are used to clean and wet the contact lens surface, especially the way in which these solutions can influence the contact lens material interaction in the eye and tear film. This thesis will investigate the interaction of solid-liquid interfaces between the eye and the lens.

Contact lens surface wettability can be measured using contact angle methodologies, such as sessile drop and captive bubble. The wettability (the ability of liquid to wet a surface) of a surface is measured by using water as the probe solution. The angle formed between a water droplet and the lens surface is the contact angle. The smaller the contact angle measured, the more wettable the surface. Other probing solutions can also be used, such as diiodomethane and hexane. These additional probe liquids give insight into how a material surface will respond to other tear components, such as lipids. The surface free energy can also be calculated when a surface has contact angle measurements from more than one probing solution.



Figure 1.2 Schematic diagram of low and high contact angles between a droplet and surface

The surface free energy can be separated into two components, polar and dispersive. Water has a high polar component and diiodomethane has almost no polar component. The contact lens surface free energy gives an indication as to how the lens surface molecules rotate in reaction to the environment. A material with a high polar fraction will be a more wettable material.

Patents and increased process costs are limiting factors for certain companies, and continuous research is carried out into how the surface of a contact lens can be modified and if this modification is persistent over the suggested wear schedule.

Wetting agents can be used in the lens material matrix, packing solution or in the contact lens cleaning solution. Simple surfactants have hydrophobic tails and hydrophilic heads. The hydrophobic tail is attracted to hydrophobic areas on the surface of the lens, leaving the hydrophilic head effectively masking the hydrophobe.

Several surfactants are used in the current range of MPSs; sometimes more than one (see Table 4.1.1) in a given solution. All the surfactants have different molecular weights, hydrophobicities and structures. In this work triblock copolymer surfactants such as poloxamers (Pluronic®) and poloxamines (Tetronics®) are the main focus for the experimental work as these are the most common surfactants used in the ocular environment. These surfactants have three distinct polymer blocks, hydrophobic centre blocks and hydrophilic tail blocks. Their designatory numbers (e.g. F127, 1107) indicate the molecular weight and hydrophobicity of each surfactant (see section 2.1.3).

The surfactant solutions also show different surface behaviours. The surface tension of liquids can be measured by using techniques such as Du Noüy ring (static) and maximum bubble pressure (dynamic). Water has a very high surface tension (72.8 mN/m) and typical MPSs have a static surface tension of around 50mN/m. Very small amounts of surfactant can be detected in static surface tension measurements. Surfactant solution surface tension increases when measured using dynamic methods, the higher the solution agitation the higher the surface tension [7]. Dynamic methods are not as sensitive as static methods, but it is possible to predict the molecular weight

Of a surfactant by the dynamic surface tension measurements; larger molecules take longer to rearrange at the surface.

The critical micelle concentration (CMC) can also be measured using both static and dynamic techniques. As the surfactant concentration in the solution increases the surface tension reduces. The CMC is where the surface tension starts to plateau[7]. The surfactant molecules start to form micelles within the solution, rather than arranging at the surface. Micelles are organised aggregates of surfactant molecules (see Figure 1.3); the hydrophobic parts of the molecules orientate towards the centre of the structure.



Figure 1.3 Simplified schematic diagram of a singular surfactant molecule and molecular formation in a micelle [7]

Surfactants clean a lens and modify the surface of the lens (See section 1.12.1). The persistence of any surface modification by surfactants is not known. It is also unknown if there is a link between persistence and molecular weight or hydrophobicity of the surfactant. A stage-by-stage, eye model evolution is presented in this thesis. The volumes and agitation are altered to better reflect the in-eye processes.

1.1. Surfaces and Interfaces

A surface or interface can be described as the region between two homogeneous bulk phases, where there are continuous property differences. There is no fundamental difference between the terms surface and interface, however it is typical to describe a gas-liquid or gas-solid boundary as a surface and a non-gaseous boundary as an interface[7]. The thickness of this boundary can vary from a few molecular diameters to a few tens of molecular diameters[8].

The surface film of a liquid is not elastic and does not stretch it expands; by creating a new surface until the film breaks and surface tension or surface free energy is a measurement of the force required to do this [9]. Surface tension and surface free energy are essentially the same property; surface tension is typically a description of the surface free energy of a liquid. Intermolecular forces such as Van der Waals contribute to the surface free energy.

1.2. Surface Tension of Liquids

The surface tension of a liquid (γ) can be expressed in dynes/cm, erg/cm² or mN/m (mN/m is the ISO standard unit) [10] and is considered as the work required to increase the area of a surface reversibly by one unit amount[9]. For example if a strip of a surface 1cm wide is extended through an additional 1cm in length then γ Ergs work has been performed and a 1cm² of new surface has been created [9].

Water has a higher surface tension than most other liquids and the presence of surface active molecules can dramatically reduce the measured surface tension. There are several ways to measure surface tension. Static methods such as Du Noüy ring, Wilhelmy plate and pendant drop, and dynamic methods such as maximum bubble pressure and pulsating bubble. ASTM D1331-11 states the ring method (Du Noüy ring) as the standard test method to measure surface and interfacial tension of solutions of surface active agents[11]. The maximum bubble pressure method is most suitable for the investigation of surfactant behaviour in a biological system because it is the dynamic behaviour that is most important in medical applications[12].

Molecules located within the bulk of a liquid are generally exposed to equal forces of attraction; a molecule at the surface has an imbalance of intermolecular forces (see Figure 1.2.1) that will pull it towards the bulk of the liquid. This net inward pull and excess of molecular forces are why liquid systems contract and minimise their surface area and why liquid droplets in air are spherical[13].

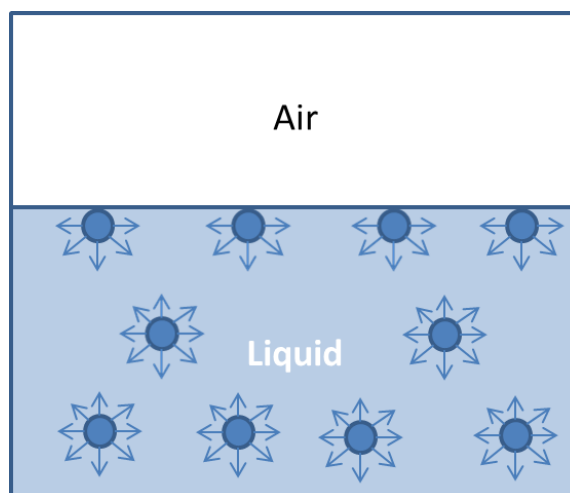


Figure 1.2.1 Attractive forces between molecules at the surface and in the bulk of a liquid [7]

All liquids have intermolecular forces such as Van der Waals (dispersive) and these are responsible for the surface tension. If hydrogen bonding (polar-water) or metal bonding (mercury) is present, then these also contribute to the surface tension.

1.2.1. Static surface tension measurement

The surface tension of a liquid can be measured in many ways and this section looks at some methods that are used under static conditions. The molecules at the surface of the liquid have an infinite amount of time to arrange themselves without any disruption.

1.2.1.1. Capillary Rise

This method involves a capillary tube being inserted into a container of liquid. The height of the liquid in the capillary tube will be different to the level in the container (see Figure 1.2.1.1.1) and the height difference between the two is used to calculate the surface tension of that liquid.

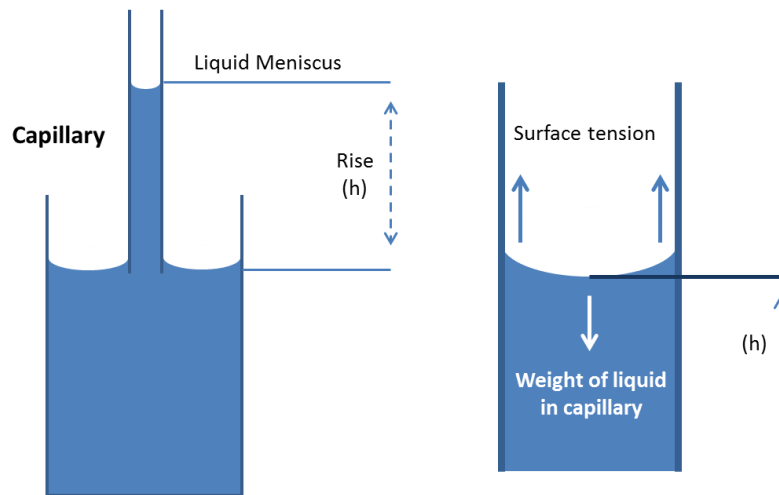


Figure 1.2.1.1.1 Capillary rise schematic[13]

In practice the capillary rise method is used only when the contact angle is zero. For the rise of a liquid up a narrow capillary (where $\theta = 0$) Equation 1.2.1.1.1 applies.

$$\gamma = \frac{1}{2} r h \Delta \rho g$$

Equation 1.2.1.1.1 [13]

Where:

γ = Surface Tension

r = capillary radius

h = rise of the liquid

$\Delta \rho$ = (density of liquid – density of gas)

g = acceleration due to gravity

An alternative method is to compare the height difference between two capillary tubes with different diameters. A possible difficulty with this method is obtaining capillary tubing with uniform radius throughout.[7]

1.2.1.2. Du Noüy ring

The du Noüy ring is one of the most frequently used techniques for measuring liquid surface tension at a liquid air interface. It is a force-based method where the pull-force of the liquid is used to calculate the surface tension[14, 15]. The ring is made of an inert material[15], such as platinum. It is suspended from a balance to measure the force readings. The container of liquid to be measured is placed on an automated platform under the balance. Figure 1.2.1.2.2 shows the du Noüy ring contact angle

with the liquid. The ring is brought into contact with the liquid surface (point 2 in Figure 1.2.1.2.1). At this point the balance registers a positive force indicating that contact has been made. The platform is then lowered slowly until the ring detaches from the liquid surface (Figure 1.2.1.2.1).

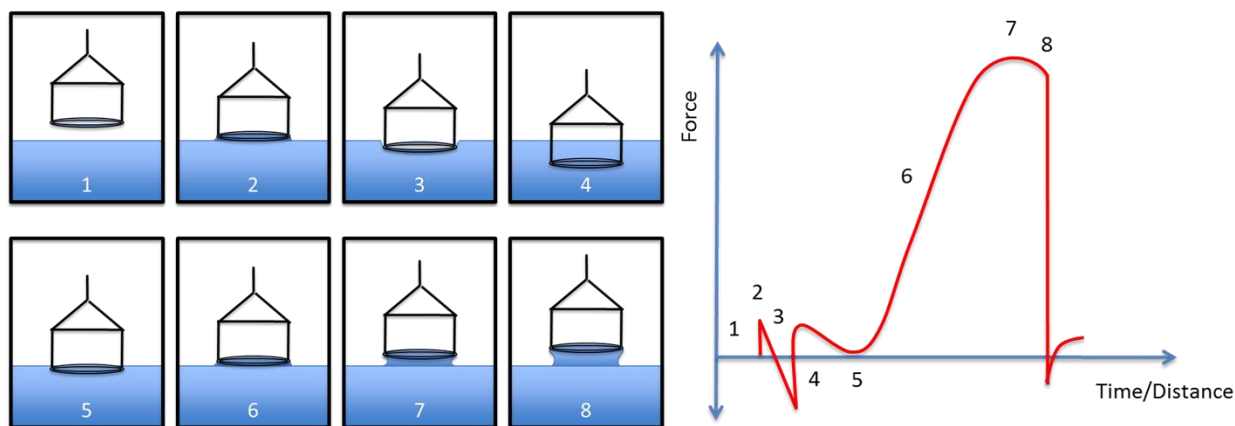


Figure 1.2.1.2.1 Progressive stages of Du Noüy ring method, with maximum force graphical representation (adapted from [16])

The point of maximum force (point 7 in Figure 1.2.1.2.1) corresponds to the liquid surface tension. The force drops slightly just prior to the surface film breaking.

This data is used to calculate the surface tension; all of the information is pre-programmed into the computer software.

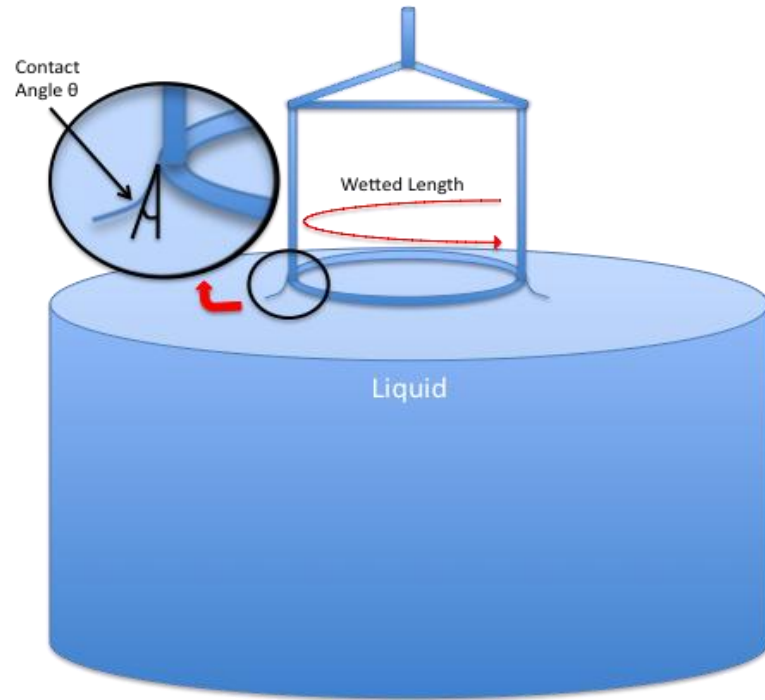


Figure 1.2.1.2.2 Schematic of Du Noüy ring contact angle

The surface tension of the solution is calculated using Equation 1.2.1.2.1.

$$\gamma = \frac{F_{\max} - F_v}{L \cdot \cos \theta}$$

Equation 1.2.1.2.1 [13, 17]

Where:

γ = Surface Tension

F_{\max} = Maximum force measured

F_v = Force at point of initial ring-liquid contact

L = Wetted length (Circumference of ring shown in Figure 1.2.1.2.2)

θ = Contact angle (see Figure 1.2.1.2.2)

1.2.1.3. Wilhelmy Plate

This method involves dipping a flat plate of inert material such as mica or platinum, through the surface of a liquid (similar to the du Noüy ring method) as shown in Figure 1.2.1.3.1. As the plate is pulled through the liquid, the downward pulling force of the liquid is measured. The liquid is thought to be completely vertical at the point where it meets the plate, so the contact angle (θ) is zero[13].

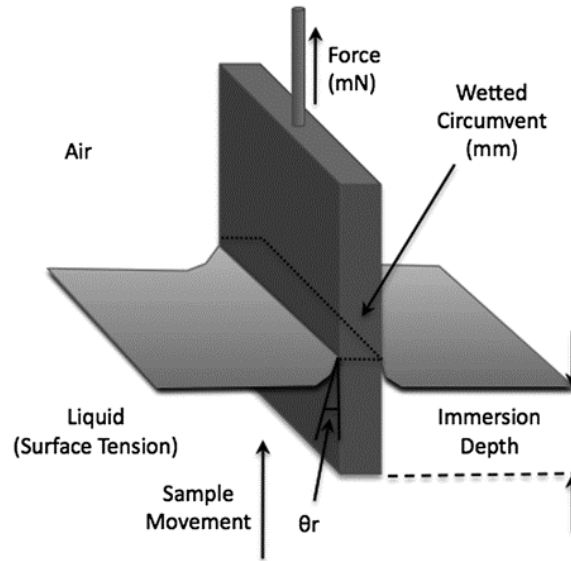


Figure 1.2.1.3.1 The Wilhelmy plate method

$$\cos \theta = \frac{F}{\gamma \cdot 2(x + y)}$$

Equation 1.2.1.3.1 [18]

Where:

F= measured force

γ= surface tension

x + y = plate dimensions

θ = Contact angle

1.2.2. Dynamic surface tension measurement

'The behaviour of interfaces under varying area conditions is affected not only by surface tension, but also by surface tension gradients, surface elasticity, and surface rheological properties'[19]

The surface tension of a liquid can also be measured under dynamic conditions, where the molecules are given a short amount of time to reorganise at the surface. The length of time can be varied and the results for different intervals give an indication into molecule size and structure.

1.2.2.1. Maximum Bubble Pressure

The dynamic method used is a pressure measurement known as the maximum bubble pressure technique[13]. The method is not effected by evaporation and equipment costs are relatively low and so it is often the method of choice when measuring dynamic surface tension.[20]

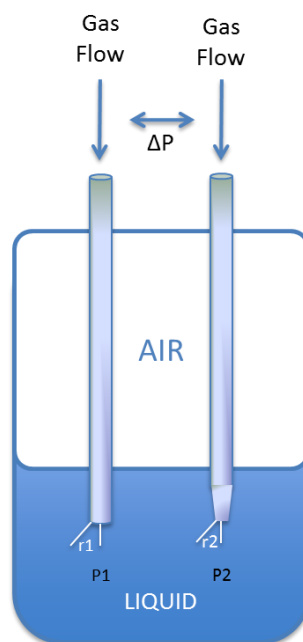


Figure 1.2.2.1.1 Maximum bubble pressure method probe configuration

The glass capillary probes are placed into the test solution and nitrogen gas bubbled through the. Bubbles are formed at the end of the tubes (point A on Figure 1.2.2.1.2 initial bubble formation) and released. Throughout the bubble formation the bubble radius changes (Figure 1.2.2.1.2), the pressure of the gas in the bubble increases to a maximum (point C on Figure 1.2.2.1.2) then decreases, until the bubble is released from the capillary tube.

This allows the software to collect pressure data and thus calculate many tension measurements over a short period of time (see Figure 1.2.2.1.2 inset). The surface tension is calculated by the software using a modified Laplace equation[13] (

$$\gamma = \frac{\Delta P}{2 \left(\frac{1}{r_1} - \frac{1}{r_2} \right)}$$

Equation 1.2.2.1.1)

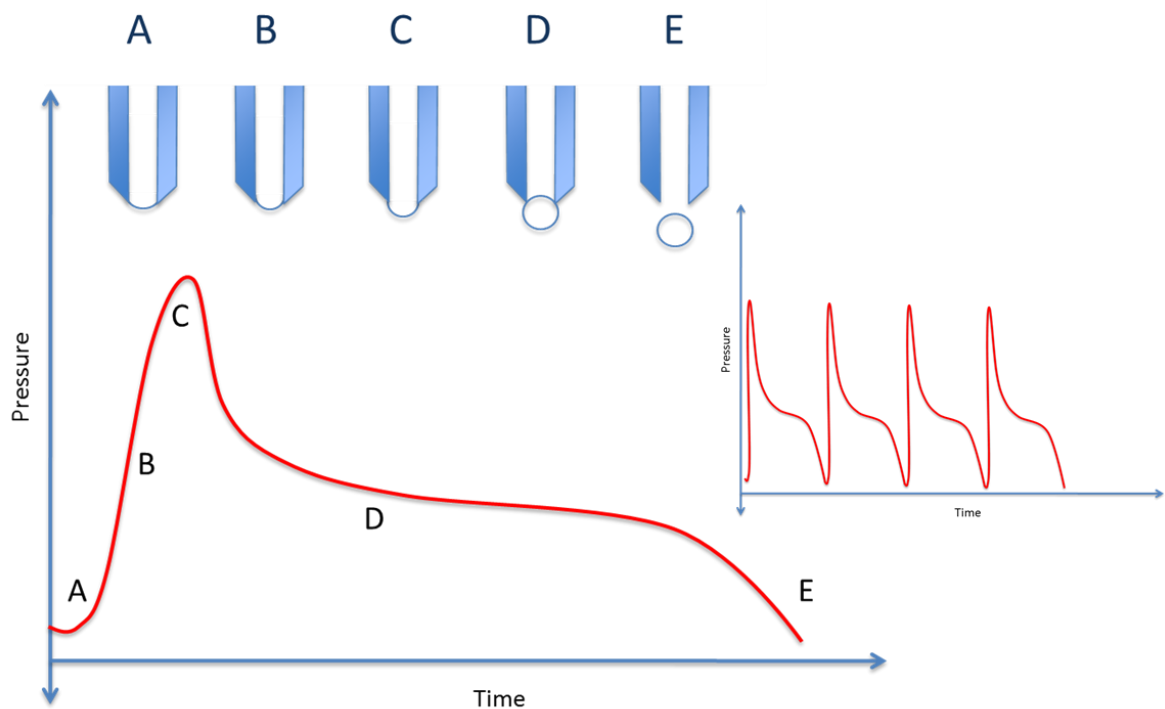


Figure 1.2.2.1.2 Maximum bubble pressure bubble radius and graphical representation (Point A shows initial bubble formation, B and C show how the radius of the bubble changes while the bubble is forming inside the tube. Points D and E show how the bubble radius changes at the end of the tube)

$$\gamma = \frac{\Delta P}{2 \left(\frac{1}{r_1} - \frac{1}{r_2} \right)}$$

Equation 1.2.2.1.1

where:

- γ = dynamic surface tension
- ΔP = pressure difference between the two probes: $P_1 - P_2$
- r_1 = radius of probe 1
- r_2 = radius of probe 2
- P_1 = pressure in probe 1
- P_2 = pressure in probe 2

1.2.2.2. Pulsating bubble

The pulsating bubble method measures the surface tension of a liquid by measuring the pressure differences across the gas/liquid interface by applying the Laplace-Young equation[19].

$$\Delta p = \frac{2\gamma}{R}$$

Equation 1.2.2.2.1

Where;

Δp = Pressure difference

γ =Surface tension

R =Capillary radius

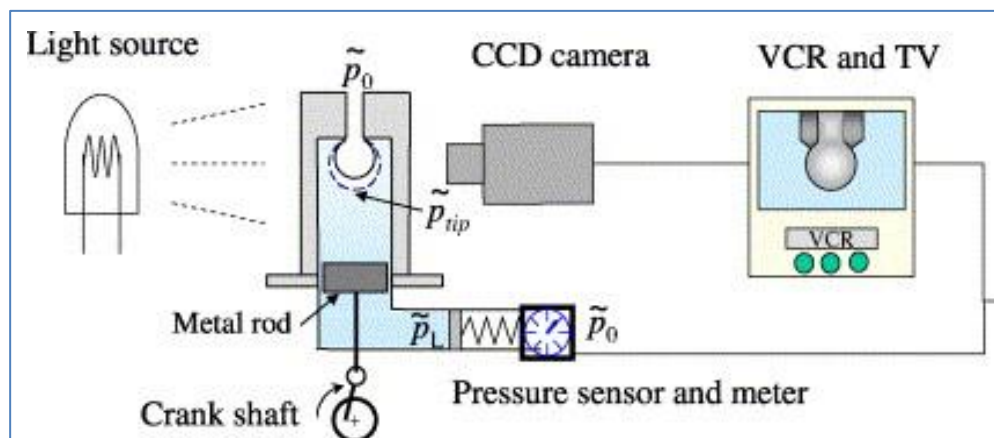


Figure 1.2.2.2.1 Schematic of a pulsating bubble surfactometer.[21]

1.2.2.3. Oscillating jet

The oscillating jet method involves a pressurised liquid being passed through an elliptical orifice. This produces a jet of liquid, the oscillating wave crests and troughs formed are dependent on the surface tension of the liquid. The surface age of each wave is determined by the flow rate of the liquid through the orifice. The lower the surface tension the longer the wave length will be.[20]

The main advantages of this method are that surface ages (age of the bubble from initial formation to when it reaches the surface of the liquid) from as little as 0.001

seconds can be measured, and surface age can be measured very accurately. This is not the case for many other methods as it is more difficult to determine when a surface is forming, whereas here the surface is formed as soon as the liquid leaves the orifice.[20]

The Bohr equation is used to calculate surface tension in this method. A simplified expression is shown in Equation 1.2.2.3.1.

$$\gamma = \frac{4\rho_1 f^2 (1 + \frac{37}{24} (\frac{b}{r})^2)}{6x\lambda^2 + 10\pi^2 x r^3}$$

Equation 1.2.2.3.1

Where:

γ = Surface tension

f =Volumetric flow rate

$r = r_{\max} + r_{\min}$

$b = r_{\max} - r_{\min}$

r_{\max} = Wave radius at antinode

r_{\min} =Wave radius at node

λ =Wavelength

ρ_1 =density of the liquid

1.2.3. Surface active agents

Surface active agents or surfactants are so called because they have hydrophilic heads and hydrophobic tails and are attracted to surfaces. In solution they form a monolayer at the surface as shown in Figure 1.2.3.1. As the concentration increases, the molecules start to form micelles. This is where the hydrophobic tails attract to each other and shield themselves from the water.

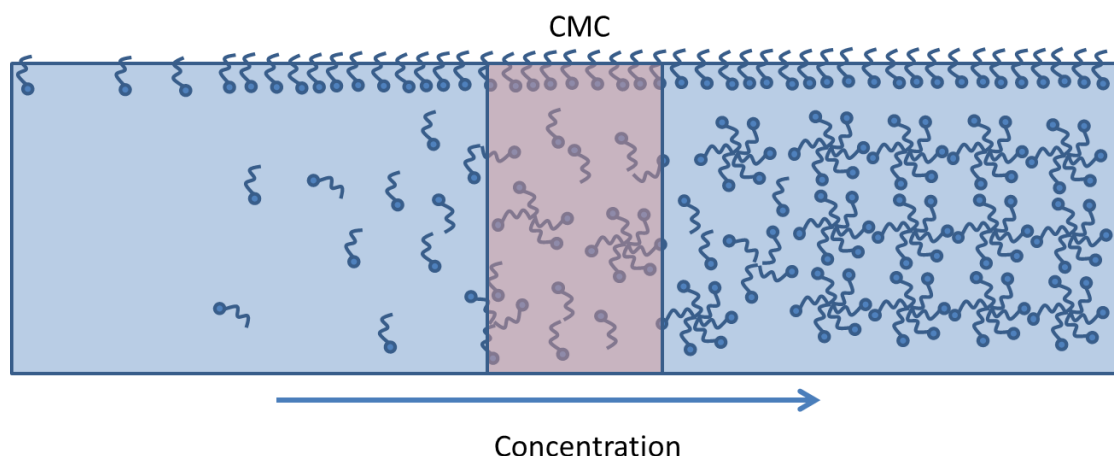


Figure 1.2.3.1 Surfactant molecular behaviour in relation to concentration

Surfactants are used for many applications, such as detergents, wetting agents, emulsifiers and so on. Surfactants are classified as anionic, cationic, no-ionic or ampholytic according to the charge carried by the surface active part of the molecule. Anionics are the most cost effective[7], cationics are the most expensive, non-ionics are unique as the hydrophile and hydrophobe chain lengths can be varied. The HLB (hydrophile-lipophile balance) number helps characterise the surfactants and helps to determine their ideal uses. They can also vary in molecular weight and molecular structure; these will be further discussed throughout the thesis. For the work presented in here, surfactant use in detergent cleaners and wetting agents in multi-purpose solutions is of most interest. For a surfactant to be able to clean it needs to be at a concentration where it can form micelles. The CMC is the point at which this starts to happen.

1.2.4. Critical Micelle Concentration

Critical micelle concentration (CMC) describes the surfactant concentration at which the surfactant monomers in solution start to form micelles. Data for a surface active solution can be collected with various physical property measurements such as osmotic pressure, turbidity; surface tension and molar conductivity, as shown in Figure 1.2.4.1.

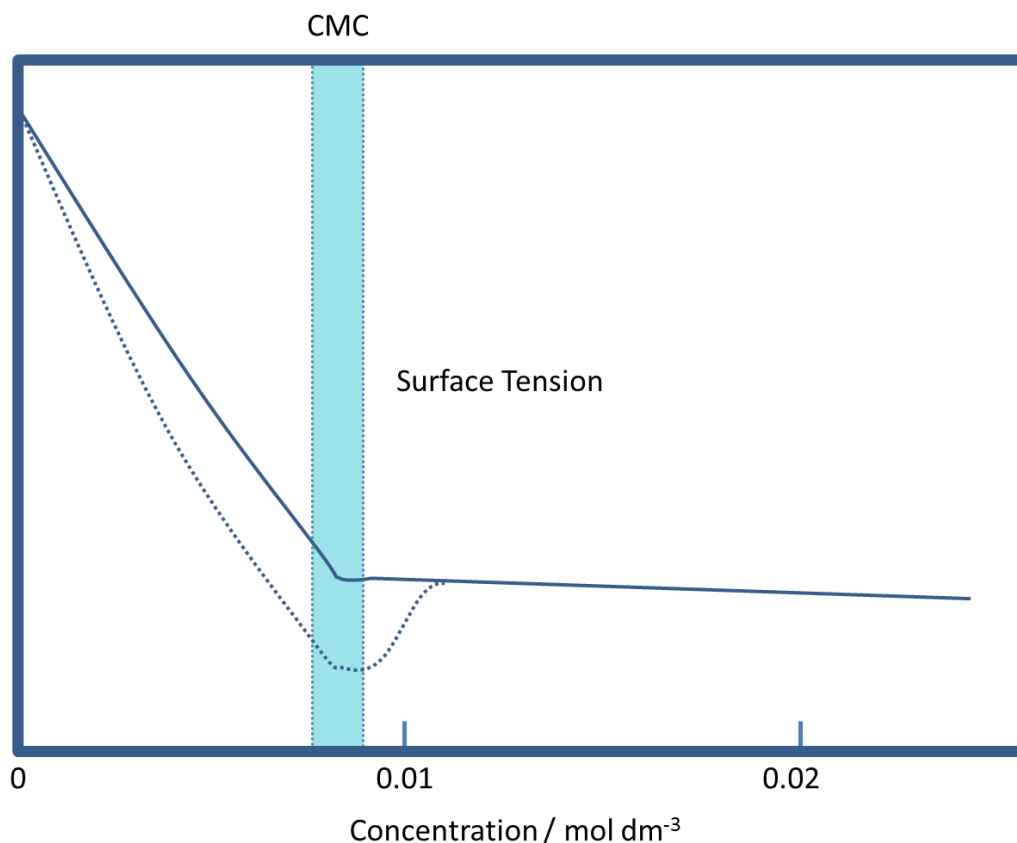


Figure 1.2.4.1 Physical properties of sodium dodecyl sulphate solutions at 25°C (adapted from [7])

This thesis is concerned with surfaces and interfaces, so the surface tension of the solution is of most interest. As the surfactant concentration is increased the surface tension value decreases. Once the CMC value is reached the changes in surface tension are minimal. CMC can be calculated by plotting the surface tension values against concentration or log concentration. In principle, the plotted data consist of two separate linear sets which intersect at the CMC and the same principles are applied to both static and dynamic data.

'micelles form not because the surfactant tails attract each other, but because the water molecules highly favour self-association over association with any solute that cannot engage in dipole or hydrogen bonding interactions' [22]

By adding surface active materials to water, the surface tension is reduced until the surface active molecules start to form micelles. This surface tension remains relatively

unchanged beyond this point because the micelles themselves are not surface active [23].

The molecular weight of a surfactant affects the CMC. The graph shown in Figure 1.2.4.2 shows the surface tension changes of the same alcohols over different concentrations.

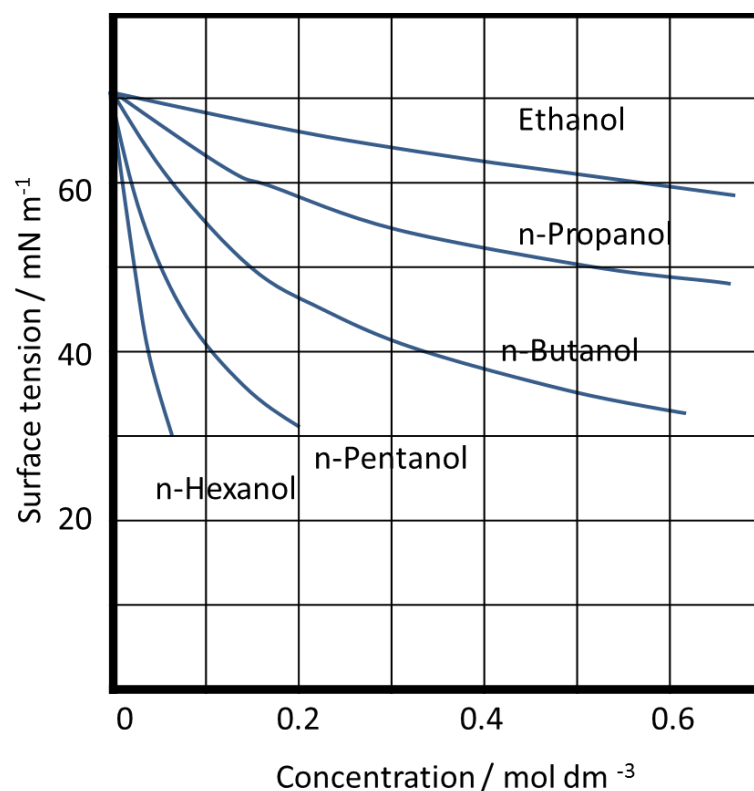


Figure 1.2.4.2 Surface tension of aqueous solutions of alcohols at 20°C (12)

Table 1.2.4.1 gives the molecular weights and carbon chain lengths of several alcohols. The alcohols with the lowest molecular weights have higher critical micelle concentrations. The CMC decreases as the molecular weight rises. According to Traube's Rule, every additional CH_2 group to the carbon chain increases the surface activity by approximately three [7].

Table 1.2.4.1 Molecular weights and Carbon Chain lengths of Alcohols

	Molecular Weight (g/mol)	Carbon Chain	Concentration at 60 mN/m*
Ethanol	46	2	0.65
Propanol	60	3	0.2
Butanol	74.	4	0.07
Pentanol	88.	5	0.02
Hexanol	102	6	<0.01

*Approximate value from Figure 1.2.4.2

Traube's law does not directly apply to poloxamers (more complex than alcohol structures) and is an approximate factor. It does however; show how important molecular weight is in determining surface activity of a solution.

1.3. Contact Angles

The basis of contact angle methodology is the angle (θ) formed at the base of a liquid drop on a solid surface (Figure 1.3.1). The angle is defined by the action of interfacial tensions imposed on the drop. Young's model described the forces, which act across these interfaces. Young's model assumes the surface is smooth, non-deformable, homogeneous, and has no hysteresis. All of these assumptions are, of course, not found in real systems[24]. As shown in Figure 1.3.1 there is interfacial tension between the liquid and gas phases (γ_{lv}), the gas and solid phases (γ_{sv}) and the liquid and solid (γ_{ls}) phases. At equilibrium these forces can be expressed by Equation 1.3.1:

$$\gamma_{sv} - \gamma_{ls} = \gamma_{lv} \cos \theta$$

Equation 1.3.1 [25] [26]

Where the angle made between the liquid droplet and the solid is θ and the liquid surface tension is γ_{lv} . Both θ and γ_{lv} can be measured which leaves γ_{sv} and γ_{ls} , as two unknowns in one equation.

Contact angles themselves are a relative value and may be useful to distinguish one material from another, but knowledge of how they are determined and what they actually mean provides a better insight into the materials. A more fundamental understanding will allow us to appreciate how materials may be interacting with their local environments. For contact lens materials this means how they interact with the ocular environment; and how they interact with cleaning and care solutions. This more fundamental understanding of surfaces begins with the surface free energy of a material.

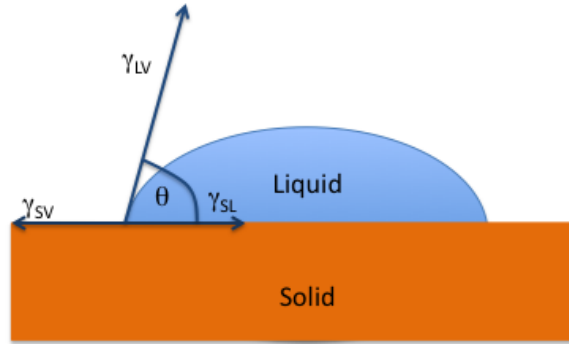


Figure 1.3.1 Schematic of a sessile-drop contact angle system. Where θ is the contact angle made between the liquid droplet and the solid, γ_{LV} is the liquid surface free energy, γ_{SV} is the solid surface free energy and the γ_{LS} is the solid/liquid interfacial free energy.

1.4. Surface Free Energy Theory

Surface free energy (SFE) is the popular term given to the interfacial tension of a solid[13]. The SFE of a material is intimately linked to contact angles formed by liquids. Young's model can act as the foundation for SFE calculations. Surface tension of liquids can be measured using several methods such as the du Noüy ring or Wilhelmy plate[7]; however a solids surface tension can only be measured indirectly.

To find the SFE of a material we begin with Equation 1.3.1, in which there are two unknowns (γ_{SV} and γ_{LS})[25]. To solve these unknowns we must first measure the angle made by a droplet, with a known surface energy, on the solid. Two liquids need to be used, one with high polarity (usually water) and one with low polarity (such as diiodomethane). The contact angles made with both these liquids and the solid are used to calculate the dispersive and polar surface energy components[25].

There are several models which allow the unknowns to be solved, and therefore to determine the SFE. These include the Fowkes-Young combining rule, the Zisman critical wetting tension, the Owens and Wendt geometric mean and the Lewis acid/base theory[27]. This thesis will look briefly at both the Fowkes-Young combining rule and Owens-Wendt models. We will describe the Fowkes-Young combining rule as it is a fundamental model, and the Owens-Wendt model as it is the most commonly used. The SFE can be split into several components as described by the Equation 1.4.1.

$$\gamma_s = \left(\gamma_s^d + \gamma_s^h + \gamma_s^{ab} + \gamma_s^p + \gamma_s^i + \gamma_s^o \right)$$

Equation 1.4.1 [27, 28]

γ_s is the total surface energy of a solid, γ_s^d is the dispersive component, γ_s^h is the hydrogen component, γ_s^{ab} is the acid-base component, γ_s^p is the polar component γ_s^i is the induced dipole–dipole component and γ_s^o includes all the remaining interactions[28].

The Fowkes-Young combining rule focuses on the dispersive component, γ_s^d , of Equation 1.4.1 as Fowkes used liquid saturated hydrocarbons as his reference materials. The intermolecular attractions in these liquids are predominantly due to dispersive surface energies and the polar component is considered to be negligible:

$$1 + \cos \theta = 2\sqrt{\gamma_s^d} \left(\frac{\sqrt{\gamma_l^d}}{\gamma_{lv}} \right)$$

Equation 1.4.2

Owens and Wendt incorporated both hydrogen (polar), γ_s^h , and dispersive surface components, γ_s^d , into their mathematical model, as they were investigating the surface energies of polymers. This resulted in the Owens-Wendt equation

$$1 + \cos \theta = 2\sqrt{\gamma_s^d} \left(\frac{\sqrt{\gamma_l^d}}{\gamma_{lv}} \right) + 2\sqrt{\gamma_s^h} \left(\frac{\sqrt{\gamma_l^h}}{\gamma_{lv}} \right)$$

Equation 1.4.3

Water and diiodomethane are often used as the probing liquids for both of these described methods. In the contact lens literature related to contact angle analysis it is only the contact angle for water (or similar polar liquids, i.e. buffers) which is commonly used.

The dispersive and polar surface energy components of the SFE for a solid are useful as they give more of indication of how a solid may behave. They provide more

information than the contact angle alone. Knowledge of the polar and dispersive components of a surface will lead to understanding on a molecular scale of how a solution may interact with that solid. For example when the surface energies are calculated for a contact lens, the polar fraction can be found (see Equation 1.4.4).

$$\gamma_p / (\gamma_p + \gamma_d)$$

Equation 1.4.4

Where γ_p is the polar surface energy component and γ_d is the dispersive surface energy component. When the SFE is calculated for a contact lens, the more polar the surface the greater the orientation of polar groups will be towards the surface for that given environment. The increase of polar groups at the surface will of course lead to a lower contact angle with water. This can be interpreted as higher wettability, which is seen as a positive feature for contact lenses. The SFE of a material will determine how it interacts in different environments, e.g. how a contact lens material interacts with the air, with buffers or with the tear film. The SFE is also linked to how a liquid spreads, which is of obvious importance for contact lens wettability.

1.5. Spreading

Spreading is an effect that occurs where a liquid is in contact with a solid. A liquid spreads to increase the liquid-solid interfacial area, and can be defined by the spreading coefficient (S), as shown in Equation 1.5.1.

$$S = \gamma_{sv} - \gamma_{ls} - \gamma_{lv}$$

Equation 1.5.1[29]

Where γ_{sv} is the solid Surface free energy, γ_{ls} , is the solid/liquid interfacial free energy and γ_{lv} is the liquid SFE. When S is 0 or positive, spontaneous spreading occurs. When S is negative the liquid stays as a drop with a defined contact angle (θ)[7] When in contact with the solid, capillary driving forces cause the droplet to spread, and for θ to move towards its equilibrium (θ_o)[29] . The speed of spreading is governed by the SFE, gravity and dissipation. If a droplet is small then gravity is negligible, small is defined

by the drop radius is smaller than the capillary length [30] the capillary length for water is 2mm [31].

1.6. Critical Surface tension

Zisman et al [32, 33] plot the surface tension of a series of liquids against the cosine of the contact angle of a sessile drop of the liquids on a polymer surface. Extrapolation of the graph to $\cos \theta = 1$ (θ is the contact angle as measured through the liquid) gives a surface tension value. A liquid with this value (if it existed) should completely wet the solid surface and it is this value that is called the critical surface tension of the solid[32].

1.7. Contact Angle calculations for non-ideal surfaces

The methods and calculations mentioned in this thesis thus far have assumed that the surfaces measured are ideal, uniform, homogeneous and smooth. This however is rarely the situation. Methods such as sessile drop and captive bubble measure contact angles on a very small area of a materials surface. Variations throughout the material on a macroscopic scale are not accounted for. There are several models that incorporate surface roughness and porosity. Both Adam[34] and Wenzel [35] showed that surface roughness effects contact angles. Johnson and Dettre [36] used a minimised version of the Wenzel model with a roughness ratio r and the observed contact angle to calculate the contact angle on an ideal surface (Equation 1.7.1).

$$\cos \theta_w = r \cos \theta_y$$

Equation 1.7.1

Where $\cos \theta_w$ is the observed contact angle and $\cos \theta_y$ is the contact angle on an ideal surface. The Cassie and Baxter model incorporates surface porosity[37] (Equation 1.7.2).

$$\cos \theta_{CB} = f \cos \theta_w + (1 - f) \cos \theta_{air}$$

Equation 1.7.2

Where $\cos \theta_{CB}$ is the Cassie Baxter angle and f is the fraction of the droplet in contact with the surface[37]. As water has a contact angle of 180° with air so $\cos \theta_{air} = -1$. These examples of how roughness can be treated with respect to contact angle show that if needed that the surface roughness can be taken into account.

1.8. Contact Angle Measurement Techniques

There are many methods for measuring contact angles.[38, 39] The techniques that will be described here are sessile drop, captive bubble and Wilhelmy plate. These are the most commonly used contact angle techniques when investigating contact lens surface properties. Most of the literature is centred on the use of sessile drop or captive bubble methods [40-44]. Less information is presented in the literature on Wilhelmy plate methods [18] An explanation of the methods follows, including dynamic variations for sessile drop and captive bubble (Wilhelmy plate is already a dynamic method).

1.8.1. Sessile Drop Method

Sessile drop is one of the most common techniques to measure contact angles (surface wettability) and the surface free energy of materials. It is an optical-based goniometry technique. In its simplest form this method involves a single droplet of liquid being placed onto a surface and the angle formed between them being measured. This angle is also known as the equilibrium advancing angle, as described by Zisman [32]. In practice the drop is generally formed using a computer-controlled syringe. This allows for the same sized droplet to be used reproducibly. The substrate to be measured is placed on a movable stage directly below the syringe (see Figure 1.8.1.1).

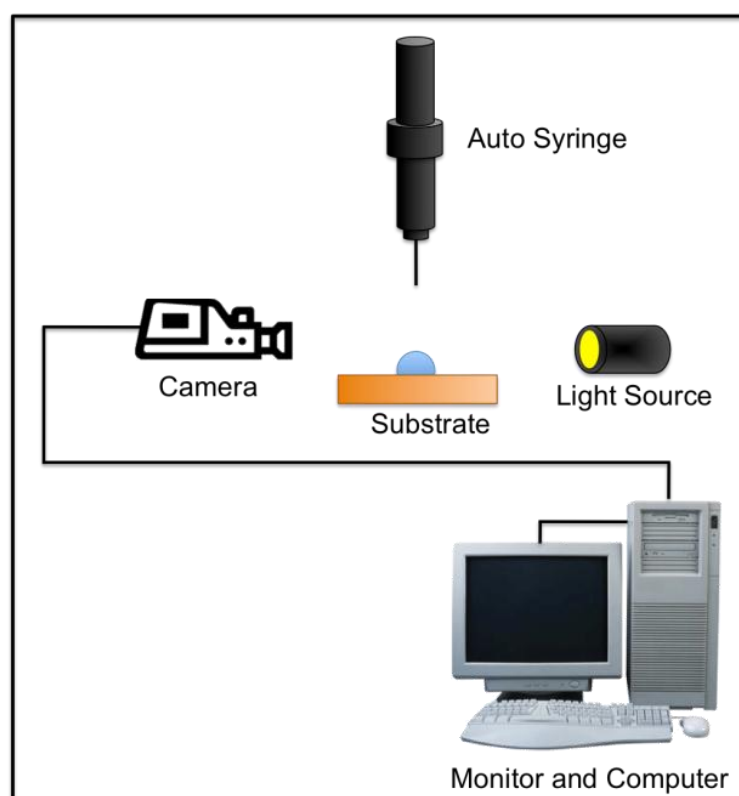


Figure 1.8.1.1 Schematic of the main elements in the sessile drop set up

A camera is focused on the stage allowing for images or videos to be taken of the drop experiment. This allows for instant contact angles to be measured and for contact angle changes to be observed over time.

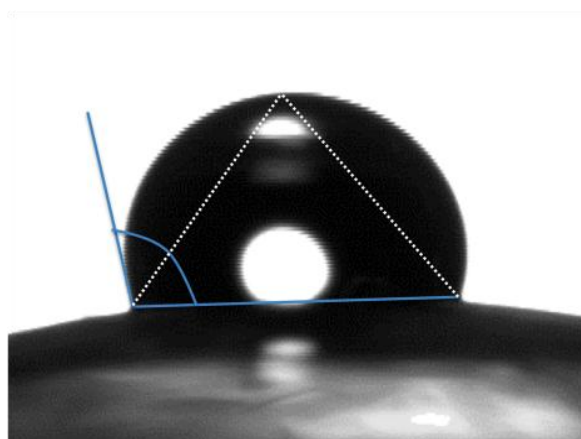


Figure 1.8.1.2 A screen-print from the DIGIDROP (GBX, FRANCE) DigiDrop software of a water droplet on a dehydrated contact lens. The solid line is the contact angle. The dotted shape represents how trigonometry is used by the software to calculate the contact angle. The sum of both angles from the base of the triangle formed is equal to the contact angle between the water droplet and the base.

In Figure 1.8.1.2 the initial drop of a solution on a contact lens is shown, note the curvature of the contact lens. The contact angle between the droplet and the contact lens can then be measured using the instruments software, an example of measurement is shown in Figure 1.8.1.2 (dotted line). If the droplet (probing liquid) used is water, then this contact angle would be an indication of the materials wettability. The wettability of a material is very useful but using more than one probe liquid allows for the SFE to be calculated. It is very important that the probe liquids used are pure; any contamination would result in angle differences. Saline and tear-like fluids would not be suitable in this case.

1.8.2. Dynamic contact angles with Sessile Drop

In addition to static contact angles, the sessile drop method can be used to measure dynamic contact angles. The measurement of dynamic contact angles by the sessile drop method is typically conducted in one of two ways; the extension and contraction method and the tilting plate method.

1.8.3. Extension and Contraction Method

This method involves placing a droplet of liquid on a surface using a syringe, and without removing the syringe increasing the volume of the drop.[36, 39, 40] Figure 1.8.3.1 shows a schematic of the extension and contraction method. When the drop is initially placed onto the surface it will have a certain base area (known as the contact line). Increasing the volume of the drop will cause this base area to increase. Prior to this the drops shape will change resulting in a change in the contact angle, which is recognised as the θ_a . The liquid in the droplet is then retracted back into the syringe. The θ_r is the defined just prior to the movement of the base line.

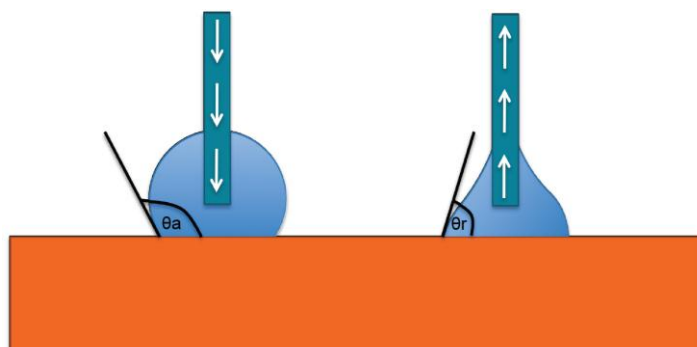


Figure 1.8.3.1 A schematic of the extension and contraction method. Arrows indicate the flow of the probing solution. The contact angles are also shown. Where θ_a is the advancing contact angle and θ_r is the receding contact angle.

1.8.4. Tilted Plate method

The tilting plate method involves tilting the platform and measuring the angles where the drop meets the platform. The method is shown in Figure 1.8.4.1. The advancing and receding contact angles of a liquid on a surface can be measured by progressively tilting the surface platform until the liquid begins to slide.[36, 39] At this point the platform has reached a critical minimum tilting angle (α crit). The θ_a is the leading angle and the θ_r is the trailing angle.

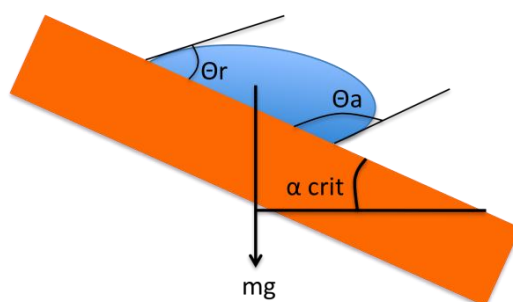


Figure 1.8.4.1 A schematic of the tilting plate method. Where α crit is the critical minimum tilting angle where the liquid just starts to move. θ_a is the advancing angle, θ_r receding angle, and mg is the force of gravity.

1.8.5. Advantages and disadvantages

The advantages of the sessile drop include; it is simple to execute, is very useful in acquiring quick results (as there is little data manipulation required), and small quantities of probe liquid can be used to perform the analysis. It can be used in

situations where force-based tensiometry is unsuitable. The method allows differentiation between contact lens material types[45].

The disadvantages of the sessile drop method include; the data obtained is somewhat subjective[45], the estimation of the angle between a drop and the lens surface is often difficult to determine, the syringe contacting the drop may affect the contact angle determined during dynamic analysis, the selection of drop size may affect the angles found, the sample is prone to dehydration, and humidity or temperature may have an effect on hydration levels of the sample.[46] For hydrogel analysis the sample preparation includes a blotting step which may affect the result. Young's model describes the droplet being measured on a flat surface; but contact lenses do not provide a flat surface. Software has been developed to incorporate lens curvature, but in practice it is quite common for the droplet to fall slightly to the side giving asymmetrical angles [46, 47].

1.8.6. Captive bubble

The captive bubble method can be thought of as an 'inverted' sessile drop method. It is also an optical-based tensiometry technique. The material is now submerged in the probing fluid (usually water) and air or an immiscible liquid are used to create the 'droplet' A U-shaped syringe is used to release air bubbles where they contact the material to form a solid/liquid interface [36, 39]. The contact angle can then be measured using a goniometer (see Figure 1.8.6.1). This method can be conducted using the same instrumentation and software as the sessile drop method. As with sessile drop if contact angles are measured using a different liquid then the SFE can be calculated.

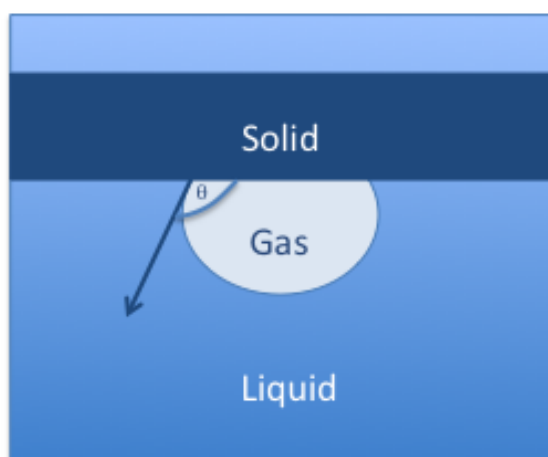


Figure 1.8.6.1 Schematic of the Captive bubble methodology[45]

1.8.7. Wilhelmy plate

The Wilhelmy plate technique is often referred to as the Dynamic Contact Angle (DCA) method. It is a force (or gravimetric) based tensiometry. A thin rectangular-shaped piece of the sample is attached to an electro balance and this is mounted above a solution. At the start of the experiment the sample is positioned in the zero force position, this is where the sample is nearly contacting the solution. The sample is then lowered, or the solution is raised, until it contacts the solution (see Section 1.2.1.3).

1.9. Contact Lens Materials

It is paramount that contact lens surfaces are visually clear, wettable, allow for sufficient oxygen transfer and to cause no damage to the eye and eyelid. Since the 1970's contact lens materials have Advanced to incorporate each of these requirements.[48]

A full historical account will not be presented here, rather a recent update from the last 10-20 years. The lens materials currently available can be categorized into several descriptions.

Hard lenses, made from PMMA. These lenses are becoming less common as they are fairly uncomfortable [49]. They do however allow for the tear film to be pumped between the lens and cornea. This enables oxygen to reach the cornea. This is very important as the cornea contains no blood vessels and needs to obtain oxygen from

the atmosphere.[50] Corneal hypoxia occurs when the cornea is starved of oxygen and can cause corneal swelling, leading to discomfort and eye redness.[51]

Rigid Gas-Permeable (RGP) lenses. Made from materials such as silicone acrylate, these have high oxygen permeability (Dk) (as their name suggests). They are also more comfortable than hard lenses [49] because in addition to their increased oxygen permeability, they are made to the specific curvature of each individual eye[52].

Soft lenses. These are currently the most common contact lenses used today.[53] Initially the lenses were made with materials based on poly 2-hydroxyethyl methacrylate (HEMA) Figure 1.9.2. Soft lenses can be further divided into; hydrogels (conventional lenses) and silicone hydrogels.

Conventional hydrogel materials adsorb high volumes of water in relation to their size, allowing the material to be very flexible and highly wettable. [53] Both of these properties increase wearer comfort when compared to RGP or hard lenses. Unfortunately hydrogel materials only allow a small amount of oxygen to reach the cornea. The oxygen permeability is directly related to the amount of water (Equilibrium Water Content (EWC)) in the lens material (see Figure 1.9.1). For practical and economic reasons however, continuously increasing the water content of a material is not an option as the lens would be too delicate to handle.

Synthetic carbon based polymer materials such as polymethylmethacrylate (PMMA) and poly(2-hydroxyethyl methacrylate) (HEMA) have been successfully used in contact lens materials. The oxygen permeability of these materials depends mainly on the water content of the material and had shown to be insufficient for maintaining a health cornea[54]. Silicone rubber has a much higher oxygen permeability (400-600 Barrers[55]) than water (100 Barrers[53]) and there has been research into incorporating this property into a contact lens material[56].

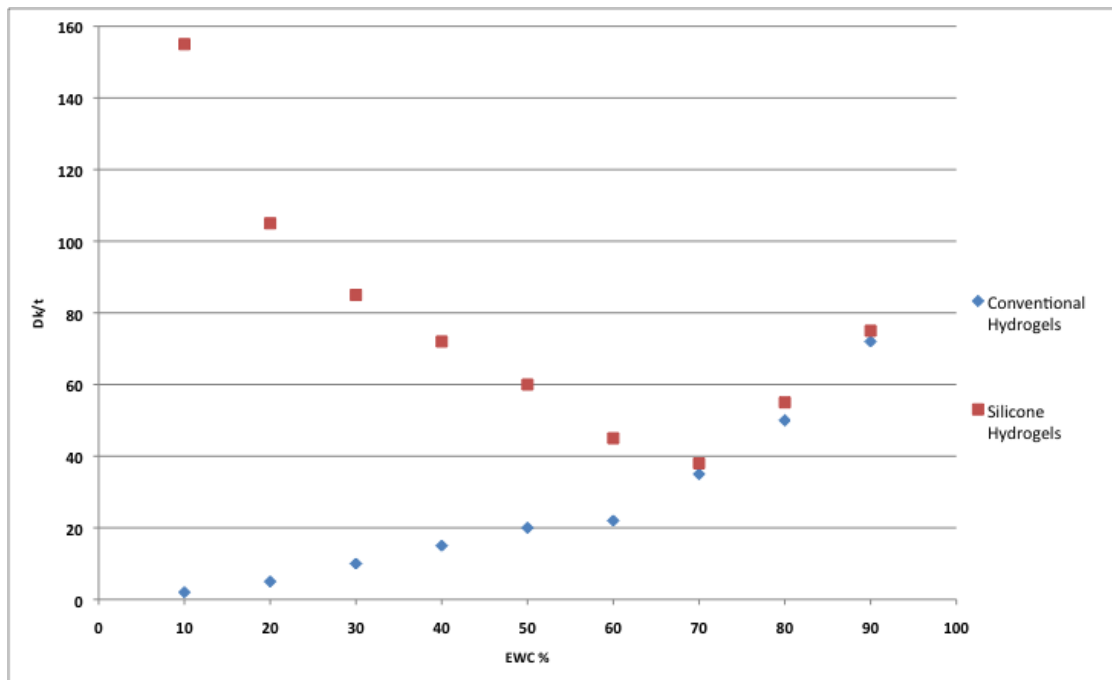


Figure 1.9.1 The equilibrium water contact vs Dk of conventional hydrogel and silicone hydrogel contact lens materials. Highlighting the Dk limitations of conventional materials [57]

Silicone hydrogel lenses incorporate the high oxygen permeability of silicone into the hydrogel material. This allows for high Dk and high EWC to be achieved. So in turn increases the comfort of the lens and the health of the cornea [57]. Silicone hydrogels contain a trimethyl siloxysilyl (TRIS) molecule. TRIS has three methacrylated trimethyl silicone groups stemming from a primary silicone group at one end and a hydrophilic monomer at the other end [53] (see Figure 1.9.2).

Figure 2.1.5.1 in Chapter 2 describes the contact lens materials and the material monomers and Figure 1.9.2 shows the monomer chemical structures

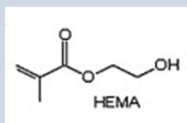
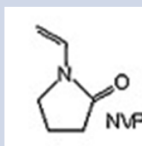
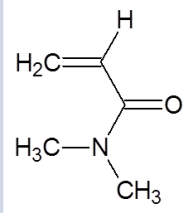
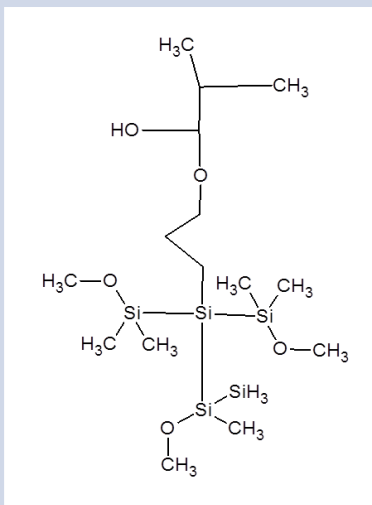
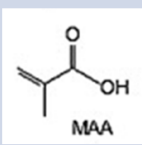
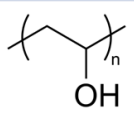
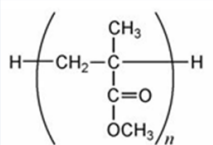
HEMA	NVP	DMA	TRIS
			
MA	PVA	PMMA	
			

Figure 1.9.2 Contact lens Material Monomers [58-61]

HEMA (Hydroxyethyl methacrylate), NVP (Vinyl pyrrolidone), DMA (dimethacrylate), TRIS (Trimethyl siloxysil), MA (Methacrylic acid), PVA (polyvinyl alcohol), PMMA (polymethyl methacrylate).

The silicone molecules are needed to transport oxygen through the lens. Silicone however is hydrophobic by nature and strives to be in a hydrophobic environment such as air. Hydrophobic domains start to form at the surface of silicone hydrogels, particularly if they are uncoated. These domains cluster together and make the polar fraction of the surface much less. Tear lipids are attracted to the hydrophobic domains. A build-up of lipid deposits on a contact lens surface can increase its hydrophobicity and make the lens less comfortable. This lipid attraction is much higher in silicone hydrogels than in conventional hydrogels[62].

1.10. Contact Lens Surfaces

The techniques described in this thesis, predominately look at the surface of the contact lens, as this is what comes into direct contact with the eyelid, cornea tear film. A more wettable and lubricious contact lens should be more biocompatible and most comfortable during wear. When contact lens materials have the desired bulk properties, such as oxygen permeability, the surface properties can fall short[63].

Further modification of the material can improve the biocompatibility of the lens; the following section describes this further.

1.10.1. Surface Modification

Surface modification can be achieved in several ways; plasma treating or coating of a lens surface, internal wetting agents added to lens polymers prior to polymerization, packing solution additives e.g. surfactants, and most recently, a hydrogel coating on a silicone hydrogel lens (see Figure 2.1.5.1).

- Plasma reaction, either to coat the surface of the lens or to change the surface chemistry. Typically oxygen plasma is used to etch the surface; this exposes hydrophilic molecules and makes the surface more wettable[64].
- Internal wetting agents and packing solution additives are hydrophilic molecules that are introduced to the contact lens material prior to polymerization or in the packing solution. Part of this thesis focuses on the latter and investigates how long this kind of surface modification lasts. See section 6.
- Hydrogel coating, Dailies® Total 1 is the first commercially available lens with this kind of modification. The wettability of a hydrogel material is obtained at the surface; a much higher EWC can be used as the silicone hydrogel material provides material strength and high Dk values[65].

Contact lens surface modification has several practical limitations, for example contact lens companies patent their manufacturing techniques. CIBA vision is the only company (see Figure 2.1.5.1) that use plasma coating to modify their lenses; this is because they have patented the technique [66]. If another company wants to use a patented method of surface modification, then royalties have to be paid to the owner of the patent. Contact lens companies have to take into account additional costs of surface modification, either by paying royalties or by adding another step to the manufacturing process. A relatively inexpensive way to modify the surface is by using wetting agents in the packing solution; however the modification is not permanent.

1.10.2. Contact Lens Wettability

Contact lens wearers who discontinue use, usually do so due to problems with discomfort and eye dryness[67]. The issue of dry eye discomfort is linked to the wettability of the contact lens surface, as the more wettable the lens the more lubrication between the eyelid and contact lens surface[68]. This reduces the discomfort caused from blinking and friction related inflammation. When a contact lens is placed into the eye it disrupts the tear film by splitting it into two parts, the pre-lens and post-lens tears films. Reducing the thickness of the tear film reduced its evaporation time. Additionally the time between blinks is increased as the post-lens tear film is relatively protected by the contact lens so the eye cannot feel the lens surface drying[69].

Also due to the nature of hydrogel polymers, the molecular chains comprising of hydrophilic and hydrophobic monomers, will rotate according to their environment [40]. So when the pre-lens tear film has evaporated the contact lens is exposed to a hydrophobic environment. The hydrophobic monomers will cause the chain to rotate, making the lens surface more hydrophobic. This increased hydrophobicity will in turn affect the lens wettability[68].

‘Lens wettability... is defined qualitatively as how well the pre-lens tear film deposits, remains stable, and recovers over the anterior lens surface’ [47]. Water contact angle measurement is usually used to investigate wettability of the lens surface, as it gives an indication of how easily the tear film would coat the lens surface.

However wettability is just one property that affects contact lens comfort. By addressing one aspect of comfort can sometimes leave other comfort factors lacking. For example, addressing the hypoxia (oxygen starvation) issue of hydrogels by incorporating silicone into the lens material also increases the hydrophobicity of a lens. By increasing the water content and wettability, the oxygen permeability of a silicone hydrogel material is reduced. Surface modification of the lenses is one way of affecting the lens wettability without compromising on Dk.

1.11. Multi-purpose contact lens care solutions: the role of surfactants

Contact lenses are placed directly on the eye, so it is very important that they are clean and sterile before they are worn. The last stage of the lens manufacturing process is sterilisation, this is commonly accomplished with an autoclave [70], but contact lenses are designed for repeated use and need to be cleaned and disinfected before reinsertion into the eye. Contact lens cleaning solutions have had to evolve to address the changing material properties of the lenses (Section 1.9) and the changing expectations of a contact lens wearer [71]. Wetting agents are also added to most contact lenses during the cleaning process; this is done to condition and modify the contact lens surface on a daily basis.

The first contact lens cleaning methodology consisted of a thermal system, enzyme tablets and distilled water. [72] Then ready-made solutions were introduced and thermal systems were replaced by cold disinfection solutions. The new solutions were easier to transport and increased the useful life of the contact lens itself.

Contact lens cleaning initially required a two-step process, cleaning and disinfection (using hydrogen peroxide), conditioning and lubrication. These solutions are very effective in removing microbes from the lens [73]. However, hydrogen peroxide is toxic to the cornea and must be removed from the lens after use or the lens would cause irritation and discomfort. This regime was reduced to a one-step regime in two ways;

- One-step hydrogen peroxide systems were created by introducing a neutralising catalyst into the contact lens case. The lenses would be left to soak in the hydrogen peroxide solution and a platinum disc at the bottom of the lens case would neutralise the solution over a period of six hours. However, if the neutralisation time was too short then the disinfection would not be sufficient to kill all microbes present on the lens [74].
- Cleaners, conditioning agents and lubricants were added to disinfection solutions, this is the foundation to the 'all-in-one' multi-purpose solutions that currently dominate the cleaning solution market today [71].

All-in-one solutions have been formulated with different disinfectants such as thiomersal, chlorhexidine, iodine and benzalkonium chloride. These disinfectants caused irritation for many contact lens wearers, so new disinfection components including Polyhexamethylene biguanida (PHMB) and Polyquaternium 1 (PQ 1) are now used. The final step with peroxide cleaning regimes is to neutralise the solution so that it can be transferred directly to the eye[75]. MPS do not require neutralisation and so need to be suitable for direct transfer to the eye.

1.11.1. Multi-purpose contact lens cleaning solutions

This section covers multi-purpose solutions (MPS) in more detail as this is currently the most popular method of cleaning contact lenses [76]. MPS are designed to clean and disinfect in one step. They can also be designed to rewet the lens surface before insertion into the eye[73]. These make the cleaning process quicker and increase the cleaning regime compliance of wearers[77]. A MPS consists of several components as they must be both effective at killing microbes, cleaning and be biocompatible with the ocular environment. Multipurpose solutions normally have three principle functions, an antimicrobial agent, a surfactant cleaner and a buffer system[73].

1.11.2. Disinfectant/Antimicrobial Agents

There are several disinfectants used in MPS at different concentrations, sometimes more than one disinfectant is used in a given solution. Antimicrobial agents used in MPS include polyhexanide biguande, polyquaternium 1, Aldox™ and Alexidine.

Polyhexanide biguande (PHMB) -PHMB is a chemical germicide used in many areas, such as sterile medical dressings and disinfection of medical and dental devices [78]. It has been used widely in the contact lens industry in varying concentrations[79].

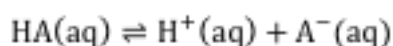
Polyquaternium 1(PQ1) is the largest polymeric molecule used for contact lenses, meaning it is not able to diffuse into the contact lens material [79]. This reduces the 'toxic hypersensitivity reactions' that can be caused by other smaller preserving molecules[79].

Aldox™ - Aldox™ is an abbreviation for aldehyde oxidase. Aldehyde oxidase produces hydrogen peroxide[80], which is very effective at killing bacteria.

Alexidine - This started as a disinfectant in the mouthwash industry and has shown to be very effective against a variety of bacteria. Works in a similar way to PHMB[79] and Polyquaternium 1.

1.12. Buffer solutions

Buffer solutions are necessary in multipurpose solutions to maintain a normal pH value (between 6 and 8) and ensure preservative effectiveness[64, 81]. The solutions can resist pH changes, even with the addition of acid and alkali. They consist of a weak acid or base and its corresponding salt, for example ethanoic acid and sodium ethanoate [81, 82] and ReNu® MPS contains boric acid and sodium borate. The behaviour of a buffer solution depends on the weak acid equilibrium.



The $\text{H}^+(\text{aq})$ stays approximately constant as there is sufficient HA(aq) to produce more $\text{H}^+(\text{aq})$ if it is used up by alkali and there is sufficient $\text{A}^-(\text{aq})$ to combine with any $\text{H}^+(\text{aq})$ that is added.[82]

1.12.1. Surfactant cleaners

The primary function of a surfactant is to clean the lens of dirt and debris they do however have a secondary benefit. Surfactants are amphiphilic and hydrophobically asymmetric molecules; they have a hydrophilic head and a hydrophobic tail; (Figure 1.12.1.1) the molecule can be attracted to both the air and the water. [19] This means they like to stick to surfaces including the surface of a contact lens. Figure 1.12.1.1 shows the molecular structure of a surfactant on the left and a graphical representation of a surfactant molecule with a polar, water loving (hydrophilic) head and a non-polar, water hating (hydrophobic) tail on the right.



Figure 1.12.1.1 An Example of a Typical Surfactant Molecule Chemical Structure of Pentanoic Acid and Graphical Representation

Surfactants reduce the surface tension of the water and also the interfacial tensions between oil (dirt and debris) and water[77], making it easier for the oil to be removed from the surface. They can also enhance the wettability of the contact lenses as the hydrophobic tail is attracted to the hydrophobic part of the contact lens and the hydrophilic head attracts water. This in turn increases the comfort within the eye.

Figure 1.12.1.2 shows how the surfactant molecules attach to dirt and debris on a surface and by reducing the surface tension of the liquid surround the dirt, the molecules lift it from the surface.

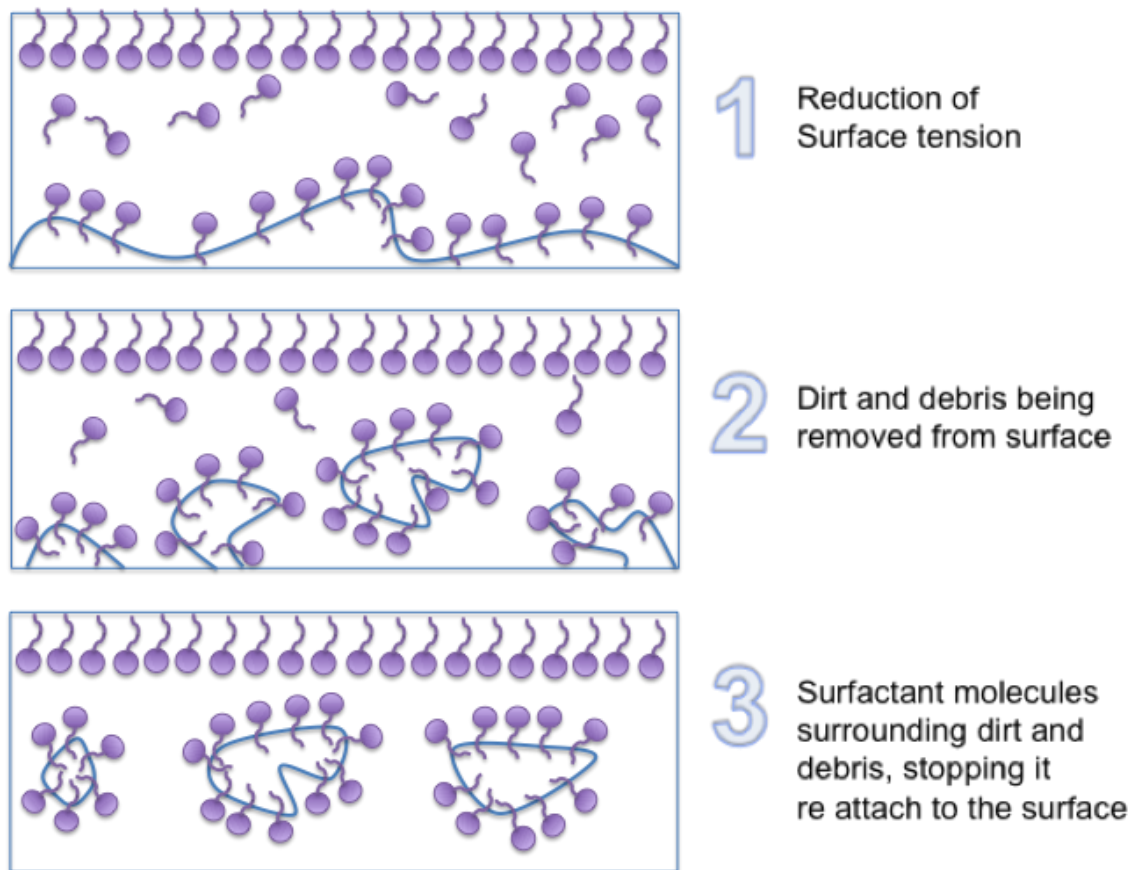


Figure 1.12.1.2 Cartoon of how surfactant molecules can remove dirt and debris from the surface and coat the surface to reduce the dirt and debris reattaching.

The molecules then surround the dirt and debris and stop it reattaching to the surface. The lens is coated with surfactant that changes the surface energy of the material and most likely making the lens more wettable[83]. The surface tension must be reduced to produce adsorption at all the surfaces that are more hydrophobic than water. In order for the molecules to not all congregate at the air/water interface, the concentration must be at or above the critical micelle concentration.

As previously stated, it is of paramount importance that the contact lens is clean enough to be worn. On the other hand it also needs to cause as little disruption to the eye as possible. Surfactant cleaners are very good at cleaning and coating the contact lens, but when placed in the eye the molecules also disrupt the lipid layer of the tear film[84]. The lipid layer stops the aqueous layer from evaporating too quickly. Small molecular weight surfactants cause more irritation than large molecular weight

surfactants[85] and for this reason, large molecular weight triblock copolymers such as poloxamers and poloxamines are most often used in contact lens MPSs.

1.13. Surfactants present in current MPS: Pluronic® (poloxamers) and Tetronic® (Poloxamines)

Poloxamines and poloxamers, trade names Tetronic® and Pluronic® respectively[77] are polyethylene oxide (PEO) and polypropylene oxide (PPO) triblock linear copolymers(9). They are present in nearly all of the currently available contact lens cleaning solutions, due to their ability to clean and rewet the surface of a contact lens, causing minimal disruption and irritation to the tear film. They are large non-ionic surfactants, it is important they have no charge because a positively charged surfactant would cause disruption to the ocular environment and a negative charge would cause the contact lens to absorb more water and swell. The structures are shown in Figure 1.13.1, both have hydrophobic PPO centres and hydrophilic PEO tails. These molecules behave similarly to the surfactants shown in Figure 1.12.1.1 and Figure 1.12.1.2. Their hydrophobic centre is attracted to the lens surface and the hydrophilic tails are attracted to water.

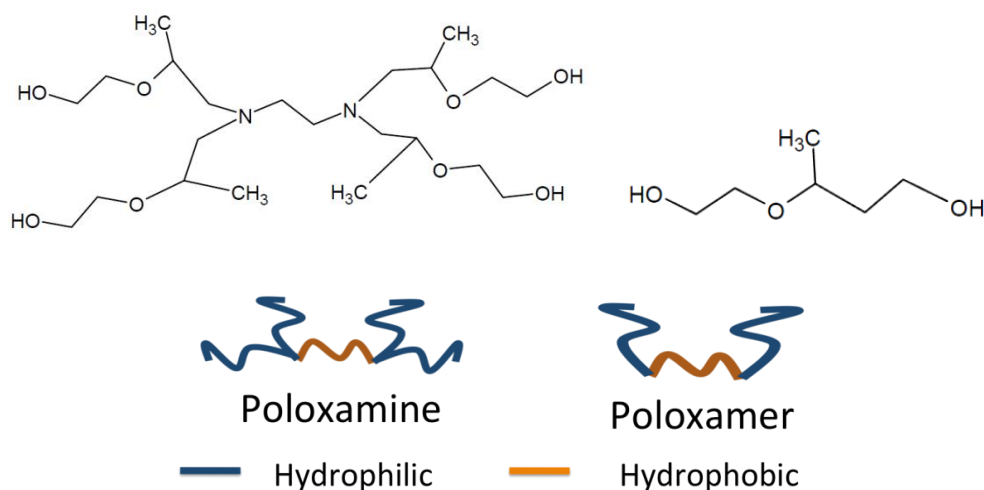


Figure 1.13.1 Tetronic® and Pluronic® Chemical structures. They are triblock copolymers with hydrophobic centres and hydrophilic tails.

There are two structural variations, the size of the hydrophobic block and the ratio of the hydrophilic (which determines the solubility of the surfactant) to the hydrophobic (which is trying to adsorb at the surfaces). In order to characterise the identity of these

surfactants we need a numerical system. This system is represented by the Pluronic grid. The grid consists of two numbers, a number to represent the molecular weight of the hydrophobic block (y-axis, PPO part of the molecule) and a number to represent the percentage of hydrophile (X-axis-PEO part of the molecule).



Figure 1.13.2 Pluronic® grid. The molecular weight and hydrophobicity of Pluronic surfactants can be calculated using this.

Pluronic® is a trade name for poloxamers. The designatory numbers are different, but it is easy to work out one from the other.

Poloxamer 188 = Pluronic® 68; poloxamer 237 = Pluronic® 87; and poloxamer 407 = Pluronic® 127.

For both poloxamers and Pluronics® the last number (e.g. 7 or 8 in the examples above) indicates the percentage of ethylene oxide blocks in the block copolymer (in the cases shown 70% or 80%). The preceding numbers (18, 23, 40, for poloxamers and 6, 8, 12 for Pluronics®) relate to the molecular weight of the surfactants by multiplying

the poloxamer prefix number by 100, and the Pluronic® prefix number by 300. So poloxamer 407 and Pluronic® 127 both refer to a copolymer with a central PPO block of 4000, and contain 70% PEO. The letter indicates the state of the poloxamers, so for F127 the 'F' stands for Flake.[86]

Tetronics® or poloxamines (eg Tetronic® 1107) are essentially 'star' arrangements of the Pluronic® structure. The final digit of the designatory number corresponds to the hydrophilic PEO block, the same as the Pluronics®. The molecular weight of the PPO block is calculated by multiplying all but the last two digits of the designatory number by 450. For example Tetronic® 1107 has a PPO block of $11 \times 450 = 4950$ (approx.) molecular weight.

Figure 1.13.3 is a simplified diagram of how poloxamers, poloxamines and surfactants attach themselves to a contact lens surface.



Figure 1.13.3 Poloxamers attached to a Contact Lens Surface

Due to their surfactant behaviour both poloxamers and poloxamines are used in many cleaning products such as hair shampoos[87] and mouthwash as well as contact lens cleaning solutions. Along with removing dirt and debris they can also increase wettability. This is done by attracting and retaining water to the hydrophilic tails, while the hydrophobic centres adhere to the surface of the. Poloxamers and poloxamines can vary in size and hydrophobicity; these properties are indicated by their names.

1.13.1. Critical Micelle Concentration of Surfactants: Pluronics® and Tetronics®

The CMC is often used to determine the suitability of a particular surfactant for specific uses, such as detergents, emulsions and surface coatings.[88]

For many surfactants increased surface tension is directly related to increased detergency (cleaning ability), and increasing CMC.[89] And in turn the more surface active the monomer is, the higher the tendency to form micelles and the lower the CMC value.[88]

Another important use for the CMC is determining which method should be used to remove excess or unwanted detergent. The literature states that detergents with high CMCs are diluted to breakdown micelles and removed via dialysis and detergents with low CMCs are typically removed by adsorption to hydrophobic beads.[90] This point is can be very useful in regards to surfactant persistence on contact lens surface if we liken the contact lens to a hydrophobic bead.

Conventional surfactants such as pentatonic acid (described in section 1.12.1) behave very similarly to Figure 1.2.4.1 in regards to CMC. Block copolymers such as Pluronics® and Tetronics® do not have such obvious CMC's. Pluronics can be denoted as PEO_m-PPO_n-PEO_m, where m and n are the number average block lengths.

CMC is influenced by the PEO and PPO block sizes, CMC increases as PEO size increases (P104 to P105) and decreases as PPO block increases (P95 to P105)[91]. The dominating factor in determining micellisation behaviour is the length of the PPO block, the PEO effect is small in comparison[92]. The hydrophobic tails of the surfactant, forces the water to form a hydrogen bonding 'cage' around the solute. The distortion of the water molecules and surfactant micelle is expected to be proportional to the surface area of the micelle. As the micelle size is determined mainly by the hydrophobic tail, the hydrophobic part of most surfactants is the dominating property contributing to CMC [22].

'The expression CMC is slightly misleading because of the use of the singular form of the word concentration'. Micelles are undetectable in dilute solutions of the monomers and become detectable over a narrow range of concentration as the total concentration of solute is increased'[88]

CMC determination in systems containing block copolymers, such as the poloxamer and poloxamine materials, can be even more difficult as the transition is not sharp and

happens over a range of concentrations.[91] These block copolymers are frequently heterogeneous with respect to both composition and molecular weight.



Figure 1.13.1.1 Variation in surface tension with concentration (log scale) for 3 Tetronics®(304, 904 and 1307 plus Pluronic® 127) (13)

The contrast between conventional surfactants and poloxamers/poloxamines can be seen by comparing Figure 1.2.4.1 and Figure 1.13.1.1 Tetronics® 904, 1307 and 304 become progressively less distinct and an inflection point very difficult to find.

1.14. The Ocular Environment and Surfactant persistence

When discussing the eye in relation to contact lens wear, the most important areas to consider are the cornea, tear film and the eyelid. For the research completed in this thesis the main area of importance is the tear film volume and turn over. The tear film thickness has been reported as between 4.2 and 24.0 μl [93], with a volume of 5-9 μl [94]. The tears are made up of at least 3 layers [3] (see Figure 1.14.1) and some research has suggested as many as 6[3].

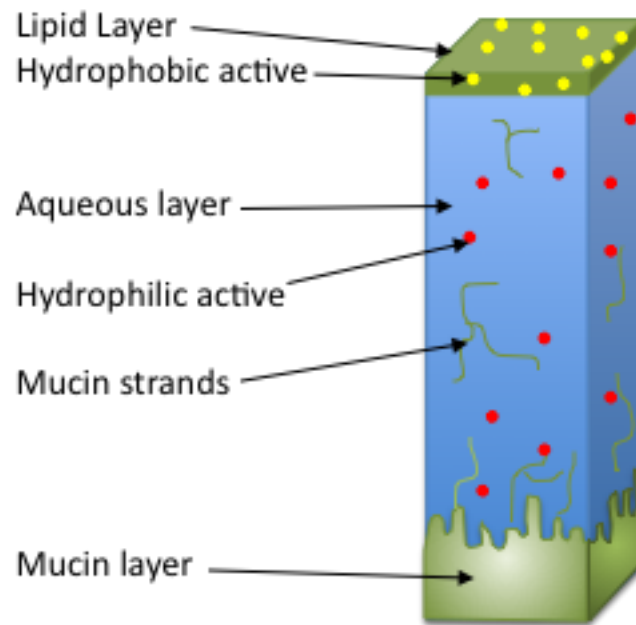


Figure 1.14.1 Three layer tear model [95]

The exterior lipid layer is produced by the meibomian glands, which are located in the above the eyelid (Figure 1.14.2). This layer helps to stabilize the tear film and prevents the aqueous layer evaporating. The lacrimal glands produce the aqueous layer of the tear film and provide most of the liquid for reflex tearing. The mucus layer is produced by goblet cells located at the conjunctiva. Mucin helps lubricate the eye and projects the epithelial surface[3]. If a foreign body enters the eye, such as a dust particle, it is quickly coated with threads of slippery mucin to protect the surface of the eye from abrasion.

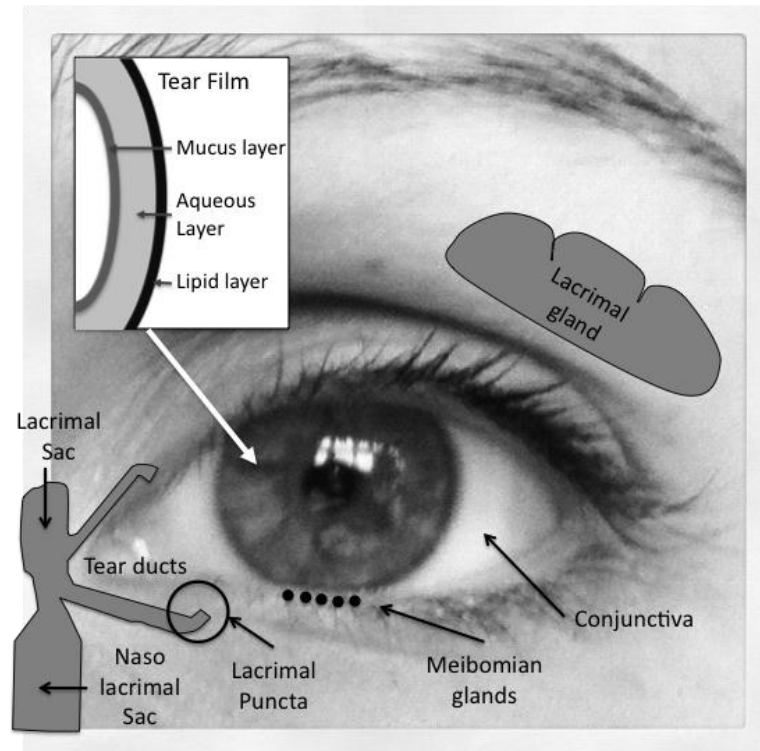


Figure 1.14.2 An Image of the eye. The glands responsible for tear production are highlighted. Inset on the image is a labelled diagram of the 3 layers of the tear film.

There are different types of tears, basal, reflex and psycho-emotional. For this work the latter can be ignored. Basal tears are the small volume of tear produced to maintain a stable lacrimal film on the surface of the cornea. This is for two reasons, to maintain corneal equilibrium and visual clarity[96]. Reflex tears are the tears produced in response to external stimuli. The volume of tears depends on the level of irritation cause by the stimuli and can range from an increase basal tear flow up to excessive tearing and tear overflow[96]. The main function of reflex tears is to wash out foreign bodies and protect and repair the ocular surface[96].

Tears leave the eye several ways, evaporation, drainage or absorption[3]. The rate, at which tears evaporate, drain or absorb, depends on the tear film composition and blink-rate and is different from person to person.

This for this work, it is being treated as a simplified input-output process. Figure 1.14.3 shows the flow diagram of the different stage blocks. Tear production is the input flow rate, the process is the coating of the surface of the eye with an average volume, and

the output is the tears that leave the eye through evaporation, drainage and absorption.

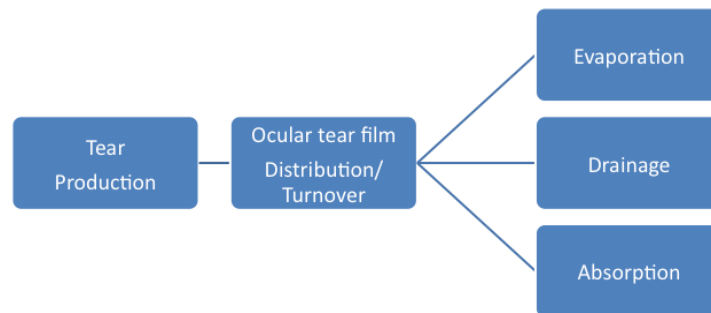


Figure 1.14.3 A Simplified process flow diagram of the tears

This simple mass balance makes it easier to create in vitro models and to evolve each model in stages.

1.14.1. The effect of Contact lens wear and surfactant surface modification on the tear film

When a lens is placed into the eye, the tear film is split into two much thinner layers, post lens and pre lens. A contact lens is approximately 0.1mm thick and much thicker than the tear film. This encourages surface dehydration of the contact lens. A dehydrated lens surface will create more friction between itself and the eyelid. This will then increase discomfort over time for contact lens wearers[97].

Surfactants are often added to contact lenses, either in the material composition or the packing solutions[98]. Any surfactant molecules that are attached to the surface of the contact lens may increase tear film attraction and increase the wettability of the lens. However if the surfactant molecules are released from the lens surface, they can disrupt the lipid layer of the tear film. This in turn will decrease tear evaporation.

1.14.2. Surfactant persistence: what is already known

Surfactants by their nature are attracted to surfaces. Contact lenses that have been treated with surfactants (wetting agents) show a lower contact angle [83] and lower coefficient of friction[99]. This surface modification is not permanent; the surfactant is removed from the surface by the tears and lid wiping.

Increasing the wettability of a lens is one factor that could improve the overall comfort of a lens and possibly reduce contact lens wearer drop out[100]. It is known that surfactants can modify the lens surface; it is not known exactly how long this modification lasts. There are several papers[18, 41] that investigate the persistence of a variety of surfactant solutions at a contact lens surface. However only one contact lens material is investigated in each study and only one contact lens cleaning solution is used in the Tonge study.

Tonge et al [18] treated etafilcon A contact lenses with 1% Tetronic® 1107 solution for 12 hours and compared them with control lenses that were soaked in saline. Subjects were asked to wear them and comfort scores taken. The dynamic contact angles of worn contact lenses were measured using a modified Wilhelmy plate methodology.

Figure 1.14.2.1 compares the dynamic contact angles for the control lenses and the surfactant treated lenses. It can be seen that the treated lenses display a lower advancing contact angle throughout the whole 500 minutes. Figure 1.14.2.2 shows the surface tension measurements over the whole experiment.

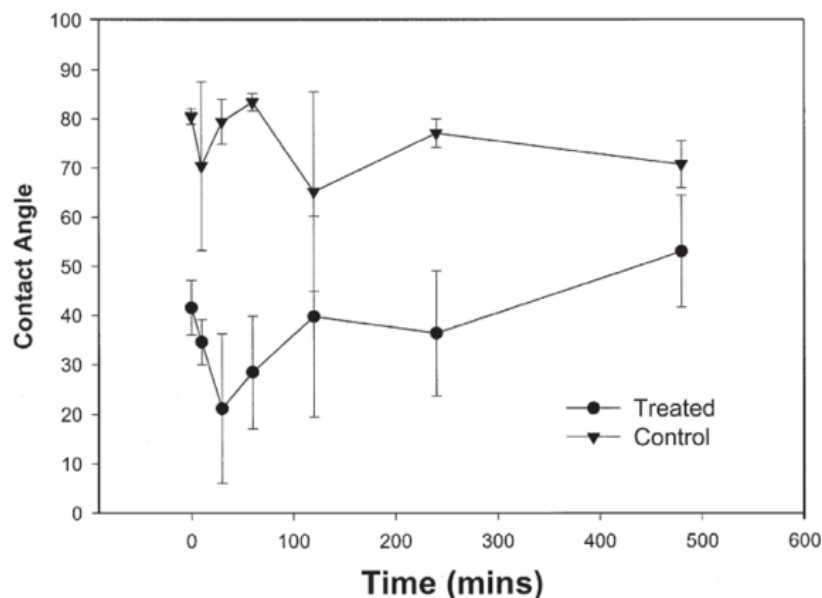


Figure 1.14.2.1 The Advancing contact angles as a function of time for treated and control lenses[18]

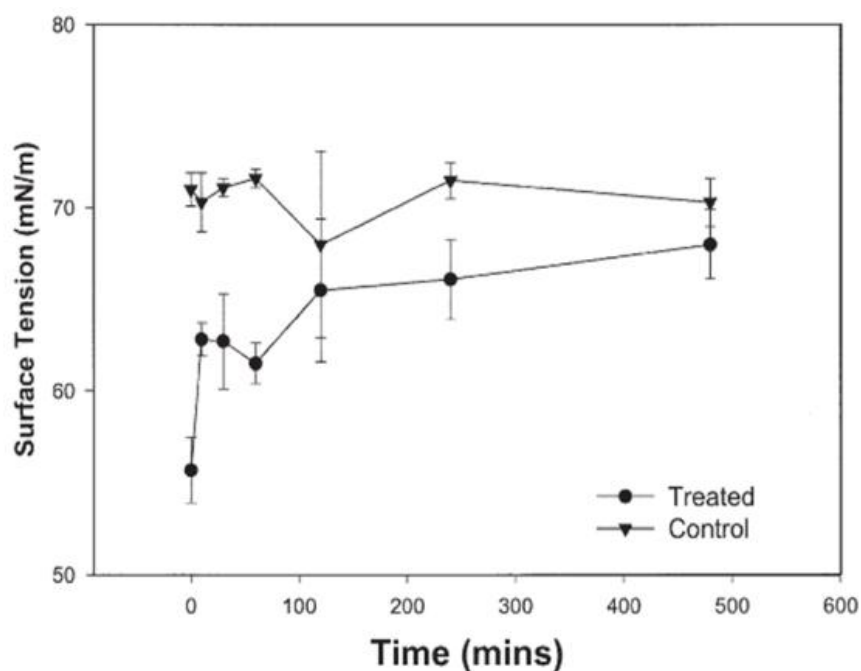


Figure 1.14.2.2 Surface tension of the probe fluid associated with the treated and control lenses over time.[18]

The Wilhelmy plate methodology requires a set volume of water of known surface tension to calculate the advancing contact angles. After each run the surface tension is measured. Both Figure 1.14.2.1 and Figure 1.14.2.2 show significant differences between the control and treated lenses. The surface tension of the probe solution seems to settle down at about 120mins for the treated lenses. However the contact angle changes seem to last until the end of the experiment.

Ketelson et al treated pHEMA-MAA (etafilcon A, Acuvue® 2) contact lenses with Tetronics® 304, 904, 1107, 1304. The lenses were soaked (treated) for 24 hours in a 0.1% surfactant solution. The lenses were then subjected to a sequential wetting and air exposure cycles. This was 'to simulate the clinical contact lens wetting and drying conditions that occur during the normal blinking process' [41] .

The contact angles and surface tension of the lens extracts were measured to analyse how long the surface modification lasted, and how much of the surfactant was being removed through the washing cycles.

This work concluded that the order of persistence from most to least persistent is T1304>T904>T304>T1107. This suggests that molecular weight and hydrophobicity of a surfactant can predict persistence behaviour.

Although these studies use different lens materials, the experiments and results complement each other. Tonge et al look at the difference between treated and untreated lenses ex vivo and Ketelson et al look at lenses in an in vitro environment and compare the effect of different surfactants.

Despite the apparent interest there is currently only one material used with only one MPS. Etafilcon A is an anionic material and represents only a small selection of available contact lens materials. At the time of the Tonge et al study, ReNu® MPS was the most popular MPS and was the most logical choice; there are at present a range of care solutions available that incorporate many different surfactants. It is this point that leads to further investigation into surfactant interaction with contact lens materials.

1.15. Scope of Work

Contact lens materials are evolving to address several factors that affect comfort. One of these factors is wettability, which is discussed in detail in section 1.10.2. The surface of a contact lens can in principle be modified to be increase wettability by attaching surface active molecules, for example through surface active components of multi-purpose cleaning solutions. Although many types of surfactants are used in contact lens cleaning solutions and many different lenses, the only combination that has been effectively studied is the anionic material etafilcon A, in conjunction with the nitrogen-containing Tetronic surfactant 1107.

This thesis aims to extend this singular example to silicone hydrogel contact lenses, which are known to be hydrophobic and might therefore be expected to interact with the hydrophobic block of poloxamer and poloxamine surfactants. The overriding aim of this thesis is to investigate the interaction between hydrogel and silicone hydrogel contact lens materials and multi-purpose care solutions; in particular the persistence of surface-active ingredients contained in multi-purpose solutions on different contact lens materials. The work will therefore entail the characterisations of lens material

surfaces and poloxamer and poloxamine surfactants. Because of the difficulties involved in in vivo work, laboratory-based experimental models will be needed. Chemical engineering modelling principles and techniques will be used to create a simplified mass balance approach to the ocular environment, to further understand these complex interactions. One important goal is to enable improved contact lens and lens care systems to be designed through understanding of existing systems.

There are therefore three variables that are involved in this study, the material, surfactant and the in-vitro eye model. It is the intention, wherever possible, to develop new techniques and a new approach to each aspect of the study.

Chapter Two

Methods and Materials

2. Methods and Materials

This chapter details the techniques and methods used to prepare and analyse the contact lens surface and to measure surface tension. In addition, information on the contact lens materials and surfactants is also presented.

2.1. Surfactants, Solutions and Contact lenses

All reagents used are shown in Table 2.1.3.1 and Table 2.1.4.1 below

2.1.1. Surfactant-containing Multi-Purpose Solutions

2.1.2. Table 2.1.4.1

All solutions were made using HPLC water.

Surfactant	Molecular Weight (g/mol)	Manufacturer
Tetronic 904 (1%)	6700	BASF
Tetronic 1107 (1%)	15000	BASF
Tetronic 1307 (1%)	18000	BASF
Tetronic 1304 (1%)	10000*	UNKNOWN
Pluronic F68LF (1%)	8400	BASF
Pluronic F127 (1%)	12600	BASF
Pluronic F108 (1%)	14600	BASF
Pluronic P65 (1%)	3400	BASF
Pluronic F87 (1%)	7700	BASF
Poloxamer 188 (1%,5%)	8400	UNKNOWN
Pluronic L64 (1%)	2900	BASF

*Calculated from grid in Figure 2.1.3.1

Poloxamer and poloxamine are generic terms for these surfactants, whereas Pluronic® and Tetronic® are BASF® trade names.

Throughout this document Pluronics® such as Pluronic® F127 will be shortened to F127 and Tetronics® such as Tetronic® 904 will be shortened to 904.

2.1.3. Surfactants

Table 2.1.3.1 Surfactant name, molecular weight and supplier



Figure 2.1.3.1 Pluronic® and Tetronic® grids from BASF®

Figure 2.1.3.1 shows the Pluronic® and Tetronic® grids and the identity of commercially available examples are shown in Table 2.1.4.1. As explained in section

1.13, the percentage hydrophobicity of the molecule is on the x-axis and the molecular weight of the hydrophobe is on the y-axis. The smaller hydrophobic molecules are soluble and are more aggressive surfactants that break up the lipid layer of the tear film. The larger molecules have a larger hydrophobic centre, a larger surface area to attach to the surface of a contact lens therefore; larger molecules should be more persistent at the surface.

2.1.4. Surfactant-containing Multi-Purpose Solutions

Table 2.1.4.1 Multi-Purpose Solutions: Brand name, surfactant, Concentration, Buffers and manufacturer.

MPS	Surfactant	Conc (%)	Buffer	Manufacturer
Complete Easy Rub	poloxamer 237	0.05	Phosphate	AMO
Complete Revitalens	Tetronic 904		Sodium Borate Decahydrate and Boric Acid	AMO
All in One Light	Pluronic F127			Sauflon
Comfort Vue	Pluronic F127			Sauflon
Opti Free Express	Tetronic 1304		Borate/Sorbitol /Aminomethylpropanol	Alcon
Synergi	Pluronic F127			Sauflon
Opti Free Replenish	Tetronic 1304		Borate	Alcon
ReNu Multiplus	Tetronic 1107	1.00	Sodium Borate and Boric Acid	Bausch + Lomb
Biotrue	Tetronic 1107		Sodium Borate and Boric Acid	Bausch + Lomb

2.1.5. Contact lenses

Manufacturer	Commercial name	USAN name	EWC (%)	Material Monomer	Material modifications	Modulus (MPa)
Bausch + Lomb	Purevision	balafilcon A	36		Plasma oxidation	1.1
Bausch + Lomb	SofLens 1 Day	hilafilcon A	59	HEMA, NVP		0.24
Bausch + Lomb	SofLens 38	polymacon A	38	HEMA		0.5
CIBA Vision	Air Optix	lotrafilcon B	33		Plasma coating	1.0
CIBA Vision	Air Optix Aqua	lotrafilcon B	33		Plasma coating & CP845	1.0
CIBA Vision	Dailies	nelfilcon A	69	PVA		0.7
CIBA Vision	Dailies All Day Comfort	nelfilcon A	69	PVA	Additional PVA	0.7
CIBA Vision	Dailies Aqua comfort plus	nelfilcon A	69	PVA	HPMC, PEG and Dual molecular weight PVA	0.7
CIBA Vision	Dailies Total 1	delefilcon A	67		Hydrogel coating 80% EWC at the surface	0.63
CIBA Vision	Focus Monthly	vilfilcon A	55	HEMA, PVP, MA		0.38
CIBA Vision	Night and Day	lotrafilcon B	24		Plasma coating	1.4
Coopervision	Avaria	enfilcon A	46			0.5
Coopervision	Biofinity	comfilcon A	48			0.8
Sauflon	Clariti	Filcon II 3	58		PVP interpenetrative network	0.5
Sauflon	Clariti 1 Day	Filcon II 3	56		PVP, interpenetrative network	0.5
Vistakon	Acuvue 1 Day	etafilcon A	58	HEMA, MA		0.3
Vistakon	Acuvue 2	etafilcon A	58	HEMA, MA		0.3
Vistakon	Acuvue Advance	galifilcon A	47		PVP internal wetting agents	0.43
Vistakon	Acuvue Moist	etafilcon A	58	HEMA, MA	Lacreon technology, PVP k90 present in packing solution prior to autoclaving to bind the molecules to the bulk and surface of the lens	0.3
Vistakon	Acuvue Oasys	senofilcon A	38		PVP	0.72
Vistakon	TruEye	narafilcon A	46		Water soluble process, PVP	0.66

Figure 2.1.5.1 Commercial contact lenses used for dehydrated contact angle, surface free energy and persistence experiments [101-105]

2.2. Preparation of solutions

Surfactant solutions were prepared using HPLC grade water and Pluronic® or Tetronic® paste, powder or flakes. For persistence experiments 1% solutions were used.

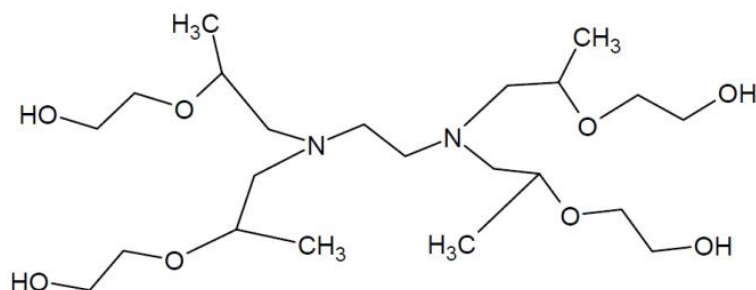


Figure 2.2.1 Tetronic® Chemical structure

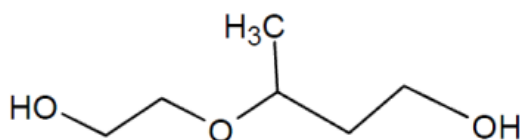


Figure 2.2.2 Pluronic® Chemical structure

2.3. Sample Dehydration

Contact angles obtained using the sessile drop technique are very common in biomaterials and contact lens literature. The samples tested are usually in a hydrated condition as they would be when in contact with the body. Using hydrated samples however, may lead to increased variation in results.

By exposing the samples to a 'dry' environment, non-uniform dehydration can occur between the samples. This means the surface water content of the samples can be altered and is an unknown factor. Hydrated samples also produce lower contact angles that are in practice more difficult to measure than higher contact angles.

The advantages of dehydrating the samples are;

- Dehydrating the samples prior to any contact angle measurement reduces or removes the surface water variable (depending on lab humidity).

- The dehydrated samples usually produce larger contact angles that are easier to measure. There is also greater distinction between the materials.

This method is not intended to simulate contact angles and wettability in contact lens wear. It is used mainly to characterize the contact lenses and compare the materials.

2.3.1. Dehydration Methodology

The contact lenses were dehydrated as follows:

Each lens was removed from the blister pack and packing solution using plastic tweezers. The lens was placed on filter paper and blotted, then set onto a curved mould. Another curved mould was placed on top to hold the lens and stop it becoming inverted while dehydrating.

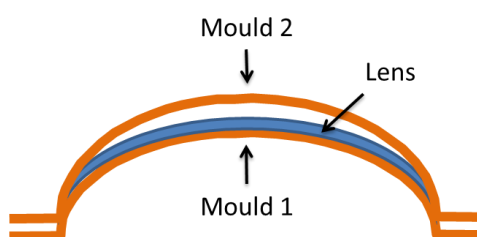


Figure 2.3.1.1 A schematic of a contact lens between 2 moulds, in preparation for dehydration.

The 2nd mould holds the contact lens only at the edge and leaves the centre (where the sessile drop measurement is taken) untouched and unmodified. The lenses were heated in a microwave on medium heat 800w for 5 minutes. The dehydrated lenses were removed from the microwave. Sessile drop contact angles (using water as the probe solution) were measured straight away. The lenses were placed into HPLC grade water to rehydrate, this also allowed for easy removal from mould 1. The lens was then dehydrated as before and sessile drop contact angles were measured using diiodomethane as the probe solution.

All lenses were disposed of after being in contact with diiodomethane.

2.4. Sessile drop technique

The sessile drop experimental set-up was as described in section 1.8.1 of the introduction. The instrument used was a DIGIDROP (GBX, FRANCE) digidrop goniometer. A photo was automatically as the drop made contact with the contact lens surface. Water and diiodomethane (a pseudo lipid) were chosen as probe solutions because water and lipoidal interactions are the most important when examining contact lens comfort. The water droplet volume was 5 μ l. This volume could not be obtained for diiodomethane due to much lower surface tension properties; the diiodomethane droplet volume was 2 μ l. Contact angles were determined as described in section 1.8.1 of the introduction, and each lens was measured in triplicate.

2.5. Surface Free Energy Calculations

As water and diiodomethane were used as probe solutions, further information can be found about the surface. The contact angles obtained from both probe liquids can be used to calculate the surface free energy of the material. The mean value from the contact angle measurements is used for both water and diiodomethane. These values are then used in the Owens-Wendt equation (see below). The polar and dispersive surface free energy components of each material can be calculated.

Owens-Wendt equation

$$1 + \cos\theta = 2\sqrt{\gamma_s^d} \left(\frac{\sqrt{\gamma_l^d}}{\gamma_{lv}} \right) + 2\sqrt{\gamma_s^p} \left(\frac{\sqrt{\gamma_l^p}}{\gamma_{lv}} \right)$$

Equation 2.5.1[25]

Below is an example calculation of a material that has an average diiodomethane contact angle of 40°. The relevant surface free energy information for water and diiodomethane is shown in Table 2.5.1.

Table 2.5.1 Surface free energy data for water and diiodomethane

Liquid	Contact Angle (θ)	γ_{lv} (d)	γ_{lv} (p)	γ_{lv} (T)

Water	60	21.8	51.0	72.8
Diiodomethane	40	48.5	2.3	50.8

Solving for diiodomethane

$$1 + \cos 40 = 2\sqrt{\gamma_s^d} \left(\frac{\sqrt{48.5}}{50.8} \right) + 2\sqrt{\gamma_s^p} \left(\frac{\sqrt{2.3}}{50.8} \right)$$

$$1.76604 = 2\sqrt{\gamma_s^d} (0.1371) + 2\sqrt{\gamma_s^p} (0.0299)$$

$$1.76604 = 0.2742\sqrt{\gamma_s^d} + 0.0598\sqrt{\gamma_s^p}$$

Rearrange for γ_s^d

$$\gamma_s^d = \left(\frac{1.76604 - 0.0598\sqrt{\gamma_s^p}}{0.2742} \right)^2$$

Solve for water:

$$1 + \cos 60 = 2\sqrt{\gamma_s^d} \left(\frac{\sqrt{21.8}}{72.8} \right) + 2\sqrt{\gamma_s^p} \left(\frac{\sqrt{51.0}}{72.8} \right)$$

$$1.5 = 2\sqrt{\gamma_s^d} (0.0641) + 2\sqrt{\gamma_s^p} (0.0891)$$

$$1.5 = 0.1282\sqrt{\gamma_s^d} + 0.1962\sqrt{\gamma_s^p}$$

Rearrange for γ_s^d

$$\gamma_s^d = \left(\frac{1.5 - 0.1962\sqrt{\gamma_s^p}}{0.1282} \right)^2$$

γ_s^d (water) = γ_s^d (Diiodomethane)

$$\left(\frac{1.76604 - 0.0598\sqrt{\gamma_s^p}}{0.2742} \right)^2 = \left(\frac{1.5 - 0.1962\sqrt{\gamma_s^p}}{0.1282} \right)^2$$

$$0.4113 - 0.053798\sqrt{\gamma_s^p} = 0.2264 - 0.00767\sqrt{\gamma_s^p}$$

$$0.1849 = 0.046128\sqrt{\gamma_s^p}$$

$$(4.008)^2 = \gamma_s^p = 16$$

So,

$$\gamma_s^d = \left(\frac{1.5 - 0.1962\sqrt{16}}{0.1282} \right)^2$$

$$\gamma_s^d = \left(\frac{0.71353}{0.1282} \right)^2 = 5.566^2 = 31$$

$$\gamma_s^p = 16.00 \quad \gamma_s^d = 31.00$$

All of the previous calculations were programmed into an Excel spreadsheet. The water and diiodomethane contact angles are input into specified cells and the polar and dispersive component values calculated automatically.

	A	B	C	D	E	F	G	H	I	J
1	dehydrated static contact angle studies									
2										
3			angle deg	angle rad	$\gamma_{lv}(d)$	$\gamma_{lv}(p)$	γ_{lv}	x	y	
4	enter data in blue	water	40	0.698132	21.8	51.0	72.8	1.529526	13.76812	
5	result in red	diiodomethane	40	0.698132	48.5	2.3	50.8	0.217767	6.441166	
6			$\gamma_s(p)$	$\gamma_s(d)$						
7	gradient	5.585600191	31.2	27.3						
8	intercept	5.22480362								
9										
10										
11	hydrated static contact angle									
12			θ (enter values below from GBX)			radians				
13		n-octane θ	145					2.530727		
14		air angle	153		27 θ'			0.471239		
15		$\gamma_{sv}-\gamma_{sw}$	64.86527							
16		γ_{sv}	92.77675							
17		$\gamma_{sv}(d)$	23.10756			64.86527	92.77675	72.8	9.338094	
18		$\gamma_{sv}(p)$	42.19376							
19		γ_{sv}	65.30132							
20		γ_{sw}	0.436041							
21										
22										

Figure 2.5.1 Screen print of the Excel spread sheet used to calculate material dispersive and polar surface energies.

The Excel spreadsheet is property of the Biomaterials Research Unit, Aston University, Birmingham.

These surface free energy component values were then plotted against several contact lens material properties, such as equilibrium water content and Dk. The graphs produced would then highlight correlations between surface free energy and material properties.

2.6. Statistical analysis

IBM SPSS software was used and two primary statistical methods have been carried out to analyse the results presented in this thesis. In simple cases where there are only two differences being considered, then a simple student t-test has been carried out. Where there are more than two differences, such as one variable with two levels, then

an ANOVA (an omnibus test) was used to show significance within the data. When significance is shown, Post Hoc Tests, least significant difference (LSD), were undertaken. The LSD test shows individual statistical differences. On one occasion a 2 way ANOVA was carried out where the two different independent variables of lens type (Silicone hydrogel, Conventional hydrogel and coated lenses) and water content (High, medium and low) were considered at different levels. In addition to the above, the Pearsons test for strength of correlation has been carried out to determine the relative strength of each.

2.7. Methods of characterisation of surfactant solutions

This thesis presents surface tension data of several Pluronic®, Tetronic® and contact lens multi-purpose solutions. Static measurements were made with a Digital Microbalance, Model DB 2 K, Whites Electrical Instruments, Malvern, England and platinum Du Noüy ring[7]. Dynamic measurements were made with the Sensodyne tensiometer, using the maximum bubble pressure method. The static surface tension gives an indication into how many surfactant molecules are at the surface. Dynamic surface tension does the same; however the surface is now continuously agitated at different bubble speeds. The surface tension changes over bubble frequency give an indication into molecule mobility and size.

Surface tension measurements (both dynamic and static) were taken, of surfactant solutions at a range of concentrations (0-1%). This was done to calculate the critical micelle concentrations.

2.7.1. Static Surface Tension Measurement – Du Noüy Ring Method, Digital Microbalance, Model DB 2 K, Whites Electrical Instruments, Malvern, England

Prior to each static surface tension measurement, the Du Noüy is cleaned using a burner and any containers were cleaned with very hot water and left to air dry. This is to remove any surface-active material that may affect the measurement.

A very sensitive balance (Digital Microbalance, Model DB 2 K, Whites Electrical Instruments, Malvern, England) is connected and controlled by surface tension

software. The platinum Du Noüy ring is attached to the suspension arm of the balance. A glass beaker of the test liquid is placed on the support platform directly below the ring (see Figure 2.7.1.1). When the ring and test liquid are in place the balance is tared.

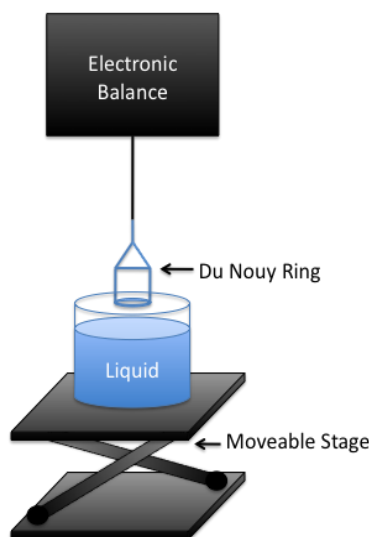


Figure 2.7.1.1 Balance and Du Noüy ring schematic

The 'Dipsurf' software (Whites Electrical Instruments, Malvern, England), which controls platform movement, is opened and set to move at rate of 0.2 mm/sec. The platform is raised manually until the Du Noüy ring is approximately 10mm above the liquid surface and the balance is tared to 0.00mN/m. The software program is started and the platform is raised until the Du Noüy ring makes contact with the liquid surface. At this point the balance registers a positive force indicating that contact has been made. The platform is then lowered slowly until the ring detaches from the liquid surface (Figure 1.2.1.2.1)

The force recorded by the balance increases as the ring emerges to the surface and reaches a point of maximum force (point 7 in Figure 1.2.1.2.1) that corresponds to the liquid surface tension[7]. The force drops slightly just prior to the surface film breaking.

The surface tension of the solution is calculated using Equation 1.2.1.2.1.

Relevant information is pre-entered into the 'Dipsurf' software and the surface tension value is shown immediately. Balance calibration was achieved by measuring the

surface tension of HPLC water (72.8 dynes/cm). Each test solution was measured 3 times. For CMC calculations this was repeated for a range of concentrations (0.02-5%).

Measured values of surface tension were plotted against (a) concentration, and (b) log concentration, to allow for the static critical micelle concentration (CMC) to be calculated.

2.7.2. Static Surface Tension Measurement - Mini Du Noüy ring (KRÜSS GmbH, Hamburg, Germany)

To measure the static surface tension of a liquid when using a standard sized Du Noüy ring, the minimum volume is 10ml. When the dimensions of the Du Noüy ring are reduced, much lower volumes can be used. A small Du Noüy ring (KRÜSS GmbH, Hamburg, Germany) and purpose made container (KRÜSS GmbH, Hamburg, Germany) were used to measure surface tension in model B. This small set up allowed for volumes as low as 200µl to be measured (see Figure 2.7.2.1)

The Du Noüy ring would be cleaned in the same way as a standard Du Noüy ring.

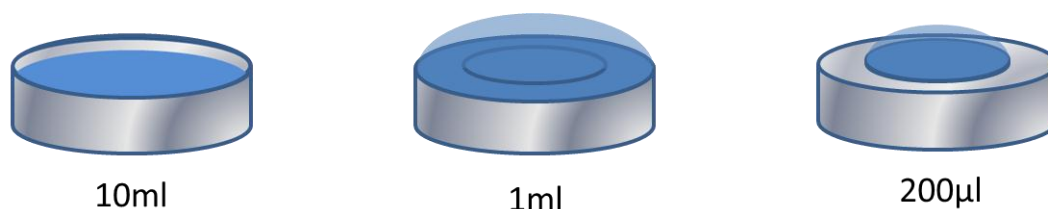


Figure 2.7.2.1 An illustration of how the purpose built container (KRÜSS GmbH, Hamburg, Germany) can be used for different liquid volumes

The container would be rinsed with hot water and rinsed again with deionised water and left to dry. Generally the container would be hot enough after rinsing, that any remaining water would evaporate straight away. When using volumes as small as 200µl the motorized platform was programmed to only allow an immersion depth of 0.5mm. This is so the Du Noüy ring or plate did not meet the container base and influence the results.

2.7.3. Maximum Bubble Pressure – SensaDyne QC3000 (SensaDyne Instrument Division, Arizona, USA)

The dynamic method used is a pressure measurement known as the maximum bubble pressure technique. The SensaDyne QC3000 (SensaDyne Instrument Division, Arizona, USA) instrument probe configuration illustrated in Figure 1.2.2.1.1 was used for these measurements.

The glass capillary probes were placed into 10ml of the test solution and nitrogen gas bubbled through them into the solution. Bubbles are formed at the end of the tubes and released. The bubble rate was adjusted to a value of approximately 3 bubbles per sec. Throughout the bubble formation the bubble radius changes (Figure 1.2.2.1.2), the pressure of the gas in the bubble increases to a maximum (point C on Figure 1.2.2.1.2) then decreases, until the bubble is released from the capillary tube.

This allows the software to collect pressure data and thus calculate many tension measurements over a short period of time (see Figure 1.2.2.1.2 inset). The surface tension is calculated by the software using a modified Laplace equation (Equation 1.2.1.2.1)

Relevant data are pre-programmed into the 'Tensiometer' software, allowing surface tension values to be automatically calculated in real time. Calibration of the technique is carried out using two liquids with known surface tensions. Calibration is performed prior to each set of experiments. In this case HPLC water (72.8 dynes/cm) and ethanol (22.4 dynes/cm) were used. The software allows real-time averaged data to be calculated as a function of time, or bubble rate. The software also facilitates transfer of data into the form of an Excel spreadsheet. Collection of multiple data points is of great value when measuring the effect of added surfactant in order to determine CMC.

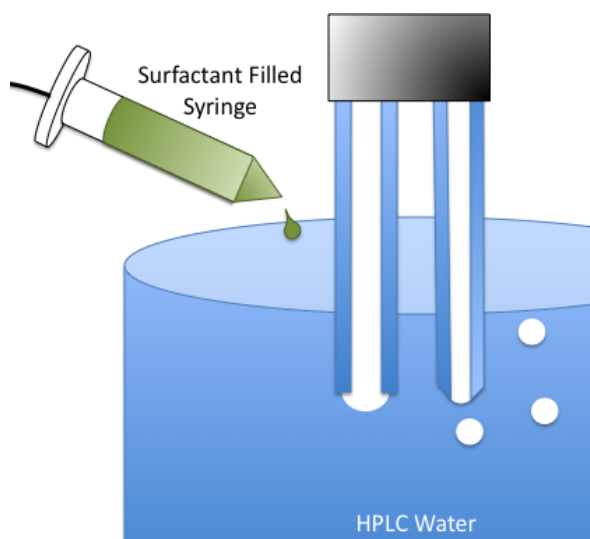


Figure 2.7.3.1 A Schematic of the dynamic surface tension maximum bubble pressure technique. Including the automated syringe for CMC measurements

2.7.4. Maximum Bubble Pressure - CMC Measurement

The critical micelles concentration is the concentration where micelles start to form and the surface tension value is no longer affected by an increase in concentration.

To calculate the critical micelle concentration, surface tension measurements are made while surfactant is added at a known incremental rate to a water reservoir (Figure 2.7.3.1). Use of a controlled delivery device (Figure 2.7.4.1) linked to the ‘Tensiometer’ software enables a plot of surfactant concentration vs. dynamic surface tension to be made.

10ml of HPLC water was used as the starting volume and concentration (equivalent concentration 0%). An automated 10ml syringe containing the surfactant solution (1% concentration) or MPS was set to dispense a pre-programmed volume over a set time. The volume of surfactant solution dispensed was measured over a 30 second period prior to experimentation to produce accurate delivery rates. The rate was input into the computer software. The standard delivery rate setting increased the surfactant concentration by 0.2% every 30 seconds. The software recorded surface tension measurements after each stepwise increase in concentration. This process continued until a pre-set concentration was reached. The data are collect in an Excel spreadsheet and converted into a plot of dynamic surface tension vs. concentration.



Figure 2.7.4.1 EFD controlled delivery device connected to the SensaDyne (SensaDyne Instrument Division, Arizona, USA) tensiometer. Syringe and container set up for dynamic CMC measurements.

2.7.5. CMC Determination - Data and Graphical Representation

CMC data for a solution can be collected with various physical property measurements such as osmotic pressure, turbidity; surface tension and molar conductivity as shown in Figure 1.2.4.1

CMC can be calculated by plotting the surface tension values against concentration or log concentration. In principle the plotted data consist of two separate linear sets that intersect at the CMC. The same principles are applied to both static and dynamic data.

In practice straight best-fit lines are drawn through the data sets and the point of intersection determined and defined as the CMC. The ability to determine the position of the CMC depends upon existence of an adequate number of data points on either side of the transition. The advantage of the dynamic technique is that more data points are collected. This is particularly useful with macromolecular surfactants, which frequently show more complex micellisation behaviour and less distinct CMC transitions than conventional low molecular weight surfactants. This point will be discussed in Chapter 4.

2.8. Contact lens surface friction

The surface of a contact lens is the focus for much of the work in this thesis and the lubricity of the material has been previously mentioned as an important factor in wearer comfort. The lubricity of the lens is directly related to its frictional behaviour.

The coefficient of friction is influenced by many factors such as substrate, load and lubricant. Changes with any one of these factors can lead to friction lubrication regime changes. There are three basic lubrication regimes, boundary layer (BL), mixed lubrication (ML) and hydrodynamic lubrication (HD)[106] (see Figure 2.8.1).

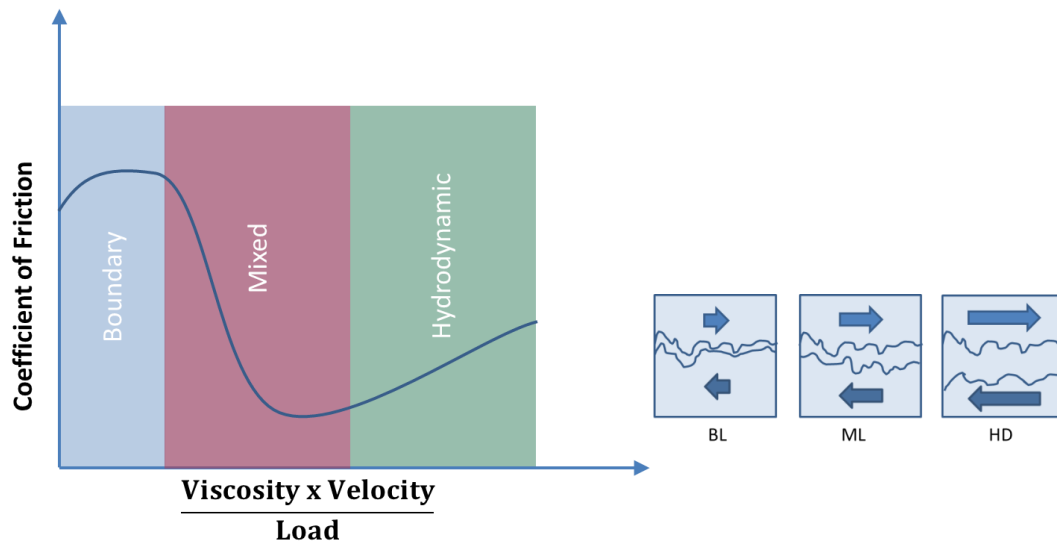


Figure 2.8.1 idealised Stribeck Curve [106] and The three basic lubrication regimes. BL (boundary layer), ML (Mixed lubrication) and HD (Hydrodynamic lubrication).

Where λ () is less than one the regime is considered to be BL, between one and three the regime is ML and over three HD. The HD regime occurs when the surfaces can be fully separated by a lubricant film, no wear ensues under these conditions and the frictional values are very low or non-measurable.[106] Mixed lubrication behaviour occurs where there is a lubricant layer but it is thin and the surfaces often come into contact with each other. The shape of the surfaces also affects the frictional performance, if they are flat then the behaviour will be less destructive than expected and if the surfaces are sharp then more wear and damage will occur. ML is a more complex regime that has many variables; the point of contact can change due to wear and the regime itself could change over time. BL regime is for λ values below 1 and the conditions here depend on surface protective layers that form at the surfaces.[106]

The Stribeck curve (Figure 2.8.1) shows the lubrication regimes and the transitions between them. For the contact lens friction analysis presented here, the viscosity, velocity and load are such that the regime is hydrodynamic lubrication. The in eye situation also simulates the hydrodynamic lubrication regime when the tear film completely coats the contact lens surface.

Tribology is the study of friction and this can be done through several methods, for example the pin on disc, calo tester and pin on slab. The pin on disc method consists of a stationary pin and a disc of the material to be tested. A load is applied to the pin, the

disc is set to rotate and the frictional forces recorded [107]. If the test material has uniform grain direction, such as wood or ceramics, there can be uneven wear of the material and this can affect the results [108]. A calo tester is more typically used to determine the thickness of a liquid coating [109] and abrasive wear resistance [43]. The pin on slab method or 'Scratch tester' is the most common method of measuring coefficient of friction. Similar to the pin on disc method, the pin is kept stationary while the sample material is moved beneath it [108].

Figure 2.8.2 shows the experimental set up of the modified scratch tester (CSM Instruments, Peseux ,Switzerland). A contact lens mould has been attached to the end of the indenter.

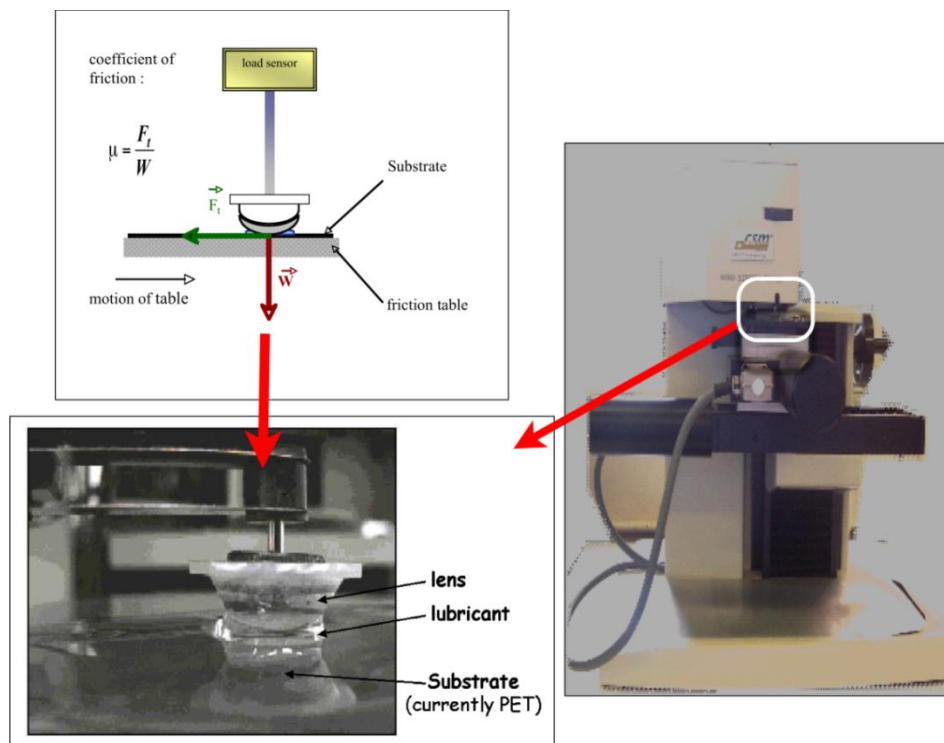


Figure 2.8.2 A schematic and photograph of the Modified Nano-Scratch Tester (CSM Instruments, Peseux ,Switzerland)

[110]

When a contact lens is tested using the above method, a friction trace is produced. From the friction trace the coefficient of friction and slip-stick value can be calculated. When soft materials slide against eye other as in the eye (eye lid and contact lens) the

slip-stick motion disturbs the expected smooth motion of the sliding surfaces. [111] An increase in friction can indicate an increase in contact lens discomfort.

The coefficient of friction is calculated with the following equation:

$$\mu = F_s/F_n$$

Equation 2.8.1

Where:

F_s = Frictional force

F_n = Applied vertical force

μ = Coefficient of friction

[112]

The friction traces contain thousands of data point per experimental run and the final COF value is an average value over at least 3 experiments.

2.8.1. Slip-Stick

For all of the frictional data presented in this work, slip-stick behaviour is present. This is where the friction traces display a saw tooth motion[113] (see Figure 2.8.1.1). Figure 2.8.1.1 shows a small section of the friction trace for a contact lens. There is clearly slip stick occurring here. The progressive increase on COF is where the contact lens material, lubricant and substrate are 'sticking' and displaying solid-like state behaviour. The slip phase follows straight after and liquid-like behaviour is observed.

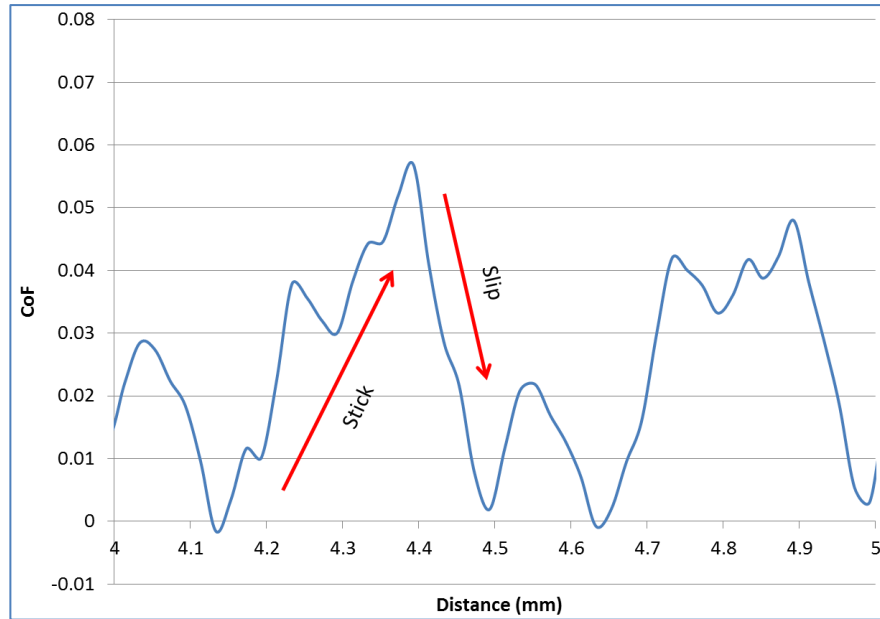


Figure 2.8.1.1 Slip and stick behaviour from a silicone hydrogel Coefficient of friction trace.

The slip stick value is calculated by firstly finding the difference between the COF of two consecutive data points (see Equation 2.8.1.1). This is done for all data points. The sum of these differences is the slip stick value.

$$SS = \sum (CoF_1 - CoF_2) + (CoF_2 - CoF_3) \dots (CoF_n - CoF_{n+1})$$

Equation 2.8.1.1

Points 1-5 in Figure 2.8.1.1 are just to illustrate the principle of slip stick calculation. There are in fact hundreds of data points in this section of the friction trace.

Slip stick is an important measurement as it is possible to have lenses with similar COF values but very different slip stick values. Slip stick is bound to influence the comfort of a contact lens as the larger slip stick with similar COF would require a higher maximum value.

2.8.2. Nano Scratch tester (CSM Instruments, Peseux ,Switzerland) methodology

A modified Nano scratch tester (CSM Instruments, Peseux ,Switzerland) was used to gain force traces that can be converted into coefficient of friction and stick-slip values

Prior to each experiment the contact lens would be briefly washed with PBS. This is to remove any excess surfactant that might be in the packing solution. The lens is blotted gently to remove surface moisture. The lens is then placed onto the underside of the Nano scratch tester (CSM Instruments, Peseux ,Switzerland) mould and left for 1 minute to air dry. The air-drying encourages the lens to adhere to the mould once a force is applied. While the lens is drying on the mould the computer software is opened to the specified experimental set up. There are several variables that can be controlled on the Nano scratch tester (CSM Instruments, Peseux ,Switzerland). For example, load exerted downwards onto the lens, the speed of sideways movement and number of passes. When the variables have been set, this can be saved as a method within the software. For example, load 30 mN, speed 30 mm/min over 10 passes, is the standard coefficient of friction method. The method will have been created well in Advance® of the experimental run and only takes a matter of seconds to select. The substrate is pre-selected and is typically PET sheeting (Melinex®) or silicone coated paper. 100ul of lubricant is dispensed with a pipette directly below the lens mould. This is again pre-selected and for these experiments was HPLC water. Once the software, lens, substrate and lubricant are ready the mould is lowered towards the substrate platform. The mould is lowered so the lens is touching the substrate. The instrument makes a warning sound if the mould is lowered too far. When everything is set and ready the software starts the programmed cycle.

The data from every pass is saved (unless programmed otherwise) as a force vs. distance trace. Each pass has 1000 data points; 10 passes have 10000 data points.



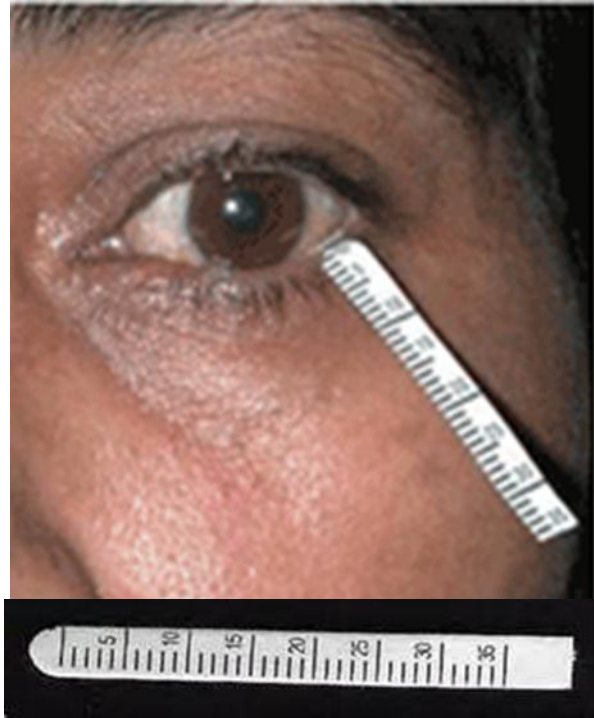
Figure 2.8.2.1 A screen print of the Nano scratch tester (CSM Instruments, Peseux ,Switzerland) software. The coefficient of friction and frictional force are shown (bottom two lines). The normal force is shown as the top horizontal line.

The software allows for all the data to be transferred to an Excel spreadsheet. Once the data is in Excel, graphs of each pass can be created and compared or a mean friction trace can be calculated over the 10 passes. In practice, passes 1-3 produce erratic results and are ignored if a mean trace is calculated. For persistence experiments, every 5 passes are recorded from 1-100 passes (20 000 total data points). When the experiment is complete, the mould is raised, the substrate sheet removed and disposed and the lens removed from the mould.

On occasion the lens edge dehydrates and cannot be removed without using force (which is avoided as the Nano scratch tester (CSM Instruments, Peseux ,Switzerland) is highly sensitive) so the lens is soaked in saline/PBS until it can be easily removed from the mould .The lens is then disposed of.

2.9. Measurement of Tear Flow Rate

There are several ways in which to take tear samples, including capillary tubes, Schirmer strips and sponge spears. Schirmer strip data was used in the assessment of individual tear flow rates (see Chapter 6).



The Schirmer strip itself is a thin strip of filter paper 35mm long that is placed so the tip is tucked underneath the lower eyelid. The strip absorbs the tears and changes colour slightly. This allows for the amount of tears to be measured in mm. The subject was fitted with the strip and asked to keep their eyes open. The experiment had two completion criteria, the tears had to either fill the Schirmer strip (35) and the time would then be recorded, or the subject was to wear the strip for 5 minutes and the tear length measured.

Chapter Three

A novel approach to the characterisation of contact lens materials: dehydrated contact angles and related properties

3. A novel approach to the characterisation of contact lens materials: dehydrated contact angles and related properties.

The scope of work contained in this thesis investigates the interaction of contact lens materials with surfactant-containing multi-purpose cleaning solutions. This includes the ‘teaming’ of a specific lens material with a specific solution. To do this it is necessary to understand and investigate the surface interactions. This chapter presents data on the inherent surface properties of commercially available contact lens materials.

The contact angle analysis (as described in Chapters 1 and 2) of hydrogel-based contact lenses is usually performed on hydrated contact lenses. Analysis of hydrated lenses is useful because the contact lenses are hydrated when worn. Surface water is an additional variable when contact angles are measured. The water at the surface of a hydrated contact lens can mask the hydrophobic nature of the surface. The surface of the contact lens dehydrates when exposed to air. This dehydration may occur at different rates for each lens and at the time of contact angle measurement the total amount of water at the surface could vary and would affect the measured contact angles. A way to reduce the effect of this variable is to remove the water from the contact lens. For the data presented in this thesis the water is removed through microwave dehydration.

Contact lens surface lubrication is very important for in-eye comfort (see section 1.10.2). A contact lens needs to be easily wettable by and completely coated by the tears on both the front and back surfaces, because the tears provide the lubrication in the eye. In order to maintain corneal physiology and lens movement, it is important that the contact lens material should have appropriate surface properties. If the tears break up on the lens surface and expose the lens to the air, dry spots can form. These dry spots encourage the silicone component in some contact lenses to attract lipids from the tear film. Lipid deposits can build up on the lens surface over time and make the surface of the contact lens increasingly hydrophobic. [114]

Contact angle techniques such as sessile drop and captive bubble are often used to investigate contact lens surfaces (see section 1.8). The most common probe solution

used to characterise contact lenses is water. There are several reasons why water contact angles are relevant in studies of this kind;

- Water is the basis for human metabolism.
- Body fluids such as blood or tears contain water and many other components including proteins and lipids.
- Water is a unique fluid with an unusually large polar fraction not matched by any other probe liquid

In addition to the hydrophilic (aqueous) interactions of a contact lens surface, it is also important to investigate the hydrophobic (lipophilic) interactions. It is possible to use a lipid substitute probe such as diiodomethane to measure lipophilic interaction. The water and diiodomethane contact angle measurements can then be used to calculate material surface energy components.

There are several studies (see Table 3.1.) in the literature that compare hydrated contact lens materials using contact angle techniques with water as the sole probe solution. The studies presented here take a further step and will calculate the surface free energies of a contact lens material.

Author	Year	Sample Preparation	Drop Vol (ul)	Water Grade	Instrument	Time before angle measurement
Read et al	2009	48 hour saline and PBS soak, solution change every 12 hours, lenses were then blotted with Supraclean microfiber cloth	3	Deionized	OCA 20 (Dataphysics Germany)	Immediate
Moldonado-Codina et al	2006	Soaked/washed for 48 hours in BBS, lenses were then blotted with a Supraclean microfiber cloth	5	Deionized	OCA 20 (Dataphysics Germany)	Immediate
Jones et al	2006	Saline rinse for several minutes	-		OCA (Dataphysics, Germany)	-
Carnell et al	2010	Short wash with PBS, surface blotted with filter paper, the dehydrated	5	HPLC	GBX digidrop goniometer	Immediate
Lorentz et al	2007	2 day PBS soak, lenses were then placed on clean lens paper for a few seconds	5	HPLC	OCA (Dataphysics Germany)	After 2-3 seconds
Santos et al	2008	Lenses cut into 4 pieces and gently blotted to remove excess moisture	-	Millipore Ultrapure	OCA 20 (Dataphysics Germany)	-

Table 3.1 Protocol comparison of sessile drop contact angle methodologies used for contact lens analysis and characteristics.[43, 115-118] (Phosphate Buffered Saline-PBS and Borate Buffered Saline-BBS)

The sessile drop contact angle method was used to acquire the data presented in this chapter because it is a convenient way to gain surface information. The technique allows for probe liquids to be interchanged easily. It is also possible for the sample to be completely dehydrated. Methodologies such as captive bubble and Wilhelmy plate are less convenient since they do not allow for different probe solutions to be used. This is because the samples are submerged in the probe solutions and are usually hydrated throughout the experiments.

When contact lenses are removed from their blister packs they are fully hydrated and are contaminated with packing solution components including surfactant. Contact angles of hydrated materials are usually low (circa 20° or less), and angles as low as this are difficult to determine. Also there is less variation between materials when there is a lot of water at the surface. The presence of water contributes so much to the surface energy that it masks the inherent properties of the contact lens material.[119]

Surfactants present at the surface of a contact lens can be removed by washing with pure water (eg HPLC grade water). A washing step is essential because surfactant contamination of the surface will affect the contact angle procedures. The ease of removal will depend on the persistence of the surfactant (which is discussed further in Chapter 6). In this work the washing step is followed by the microwave dehydration, where the water is removed in order to determine the inherent properties of the material.

Lens dehydration is not performed in order to imitate in-eye behaviours of the contact lens. It may, however, give an indication of the possible consequence of drying through daily wear. This might be referred to as the 'hydrophobic potential' the lens surface.

Diiodomethane contact angles were also measured in addition to the water contact angles. The contact angles for both probe solutions are used to calculate the surface free energy of each contact lens using the methodology described in section 2.5.

Surface energy can be split in various components as described in section 1.4. By defining the properties of the probe liquid the properties of the experimental material can be defined. For the work presented here, the most important are the polar and dispersive components because they represent the hydrophilic and lipophilic interactions of the lens with the ocular environment. To calculate the dispersive and polar surface energy values, contact angles from two different probes solutions are needed. The surface energy presents more information than the water contact angle data. The polar and dispersive components aid in the understanding of how a liquid may interact with a solid on a molecular scale.

For example, the polar fraction for a contact lens can be found using the polar surface energy component (γ_p) and the dispersive surface energy component (γ_d) (see Equation 3.1).

$$\gamma_p / (\gamma_p + \gamma_d)$$

Equation 3.1

γ_p refers to intermolecular forces that occur in all materials and γ_d refers to forces caused by permanent dipoles. The concept of polar fraction is important because it give a ration of surface polarity. It is the polar component and polar fraction that dominates the interaction between the hydrophilic components in the eye and the lens surface[45].

This chapter presents results for a range of commercially available contact lenses.

3.1. The use of probe liquids to study the surface behaviour of dehydrated contact lenses

Several commercially available contact lenses were selected for analysis and many of these are silicone hydrogel materials. Silicone hydrogels are dominated by hydrophobic siloxy and polar components, these are the two primary descriptors used in the analysis and so descriptions of polar and dispersive surface energy components (acidic or basic interactions have little impact in this family of materials) is convenient. The way in which surface energy can be subdivided into various components (polar, dispersive, acid, base etc.) is described in section 1.4. By choosing a probe liquid with defined properties, whichever of these combinations are used, the properties of the experimental study can be further described in those terms. Water and diiodomethane are ideal for this purpose. The contact lenses were dehydrated as previously described, to produce a dehydrated surface. Contact angles for both water and diiodomethane were obtained using the sessile drop technique.

Figure 3.1.1 presents the water contact angles and diiodomethane contact angles. As already discussed, the components of silicone hydrogels are predominantly hydrophobic siloxy and polar hydrophilic monomers.

The water and diiodomethane contact angles were obtained from dehydrated contact lenses.

Methodology summary:

- Lens removed from blister pack
- Placed on filter paper and blotted

- Set between two curved moulds
- Heated in microwave for 5 minutes
- Removed and tested (water contact angle)
- Lens and mould placed in HPLC water to rehydrate
- Rehydrated lens then placed in the microwave for 5 minutes, as before
- Remove and tested (diiodomethane contact angle)
- Lens disposed of

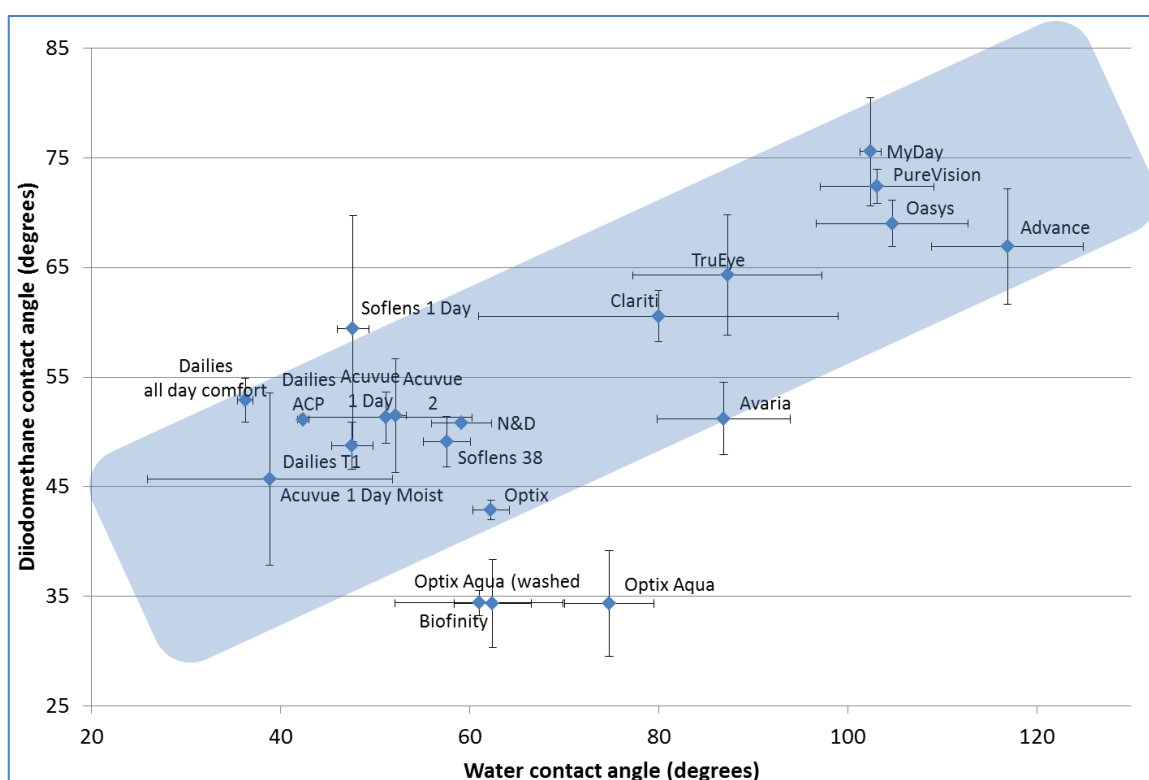


Figure 3.1.1 Water and Diiodomethane sessile drop contact angles of dehydrated contact lens materials (2009-2013)

Figure 3.1.1 shows a plot of the water contact angle against the diiodomethane contact angle obtained for each sample. Both diiodomethane and water contact angles are increasing. The general trend is that as the angles increase the total surface free energy increases. Using the Pearson test, there is highly significant correlation. Significant at the 99% level, between the water contact angle and the diiodomethane contact angle (see Figure 3.1.2).



Figure 3.1.2 Pearson Test results SPSS Software

The materials closest to the X Y intercept have the highest total surface energy. Since there is a general trend, any lenses that lie outside of this are obviously unusual. This may be because of erroneous data or atypical feature of that material. It also shows that there is a degree of coherence within these material; they show a balance between hydrophobic components and hydrogen bonding polar components.

The contact angle values here constitute the primary data for many of the calculations to follow in this chapter. Some general observations can be made from Figure 3.1.1. The water contact angles are generally more variable than the diiodomethane contact angles. It is well known that water (with its high polar component) is readily contaminated; addition of surfactants greatly reduces the surface tension. Diiodomethane is a much less polar liquid with a low surface tension; therefore contamination will not affect the surface tension to the same extent. There is some variability in the diiodomethane contact angles in Figure 3.3.1. This variability could be because the diiodomethane contact angles are generally lower than the water contact angles and low contact angles are more difficult to determine[120].

An example of water contact angle variability due to contamination is observed for Clariti® and Clariti® 1 Day lenses. These lenses show the greatest water contact angle standard deviation in Figure 3.1.1. The diiodomethane contact angles are not affected in the same way as explained earlier. The variability appears to be related to the fact

that Clariti® and Clariti® 1 Day lenses have residual PVP and VP copolymers that are readily extracted from the material[119]. These lenses are unusual as they are the only material with NVP monomer polymerised within the material matrix. This point is raised again later in the chapter.

Another example in the use of PVP is copolymer 845 is added to the Air Optix® lens packing solution; the product is marketed as Air Optix® Aqua. PVP is an amphiphilic molecule that can bind water to hydrogel based contact lens materials and increases the overall water content.[121] The copolymer is intended to increase the comfort of the contact lens. Air Optix® and Air Optix® Aqua have different surfaces then compared to other silicone hydrogel material. Their surfaces are plasma coated to create a material with a medium surface energy and to increase hydrophilicity of the surface. Copolymer 845 is prominently PVP which is amphiphilic; this means it can display both hydrophilic and hydrophobic behaviour depending on the surface and the environment. It is observed when Air Optix® Aqua lenses are dehydrated; the water contact angles are higher (unwashed Air Optix® Aqua water contact angle is 74.8°) than the original (not Aqua) Air Optix® lens (Air Optix® water contact angle 62.3°). The Copolymer 845 present at the surface is more hydrophobic than the original lens material (under dehydrated conditions). This is because the surface is already relatively hydrophilic; the hydrophilic parts of the PVP will be attracted to the surface of the lens. The surface is then masked by PVP displaying its hydrophobic components in response to the environment. The data in Figure 3.1.1 also shows that copolymer 845 is not persistent and is removed after a single wash with HPLC water and Air Optix® Aqua in-eye is effectively Air Optix® after several blinks.

Further investigation into the difference between washed and unwashed Air Optix® and Air Optix® Aqua was carried out Figure 3.1.3. The data obtained showed that the Air Optix® Aqua unwashed (under dehydrated conditions) had a lower water contact angle in contrast to what the previous results had shown. Unlike the chemical compositions of FDA approved contact lens materials (lotrafilcon A etc) the composition of packing solutions and process parameters associated with lens manufacture are not fixed. Thus a particular FDA USAN named product might change

in its apparent or ex-packing properties over a period of years. Even though the chemical composition of the core materials is fixed[119].

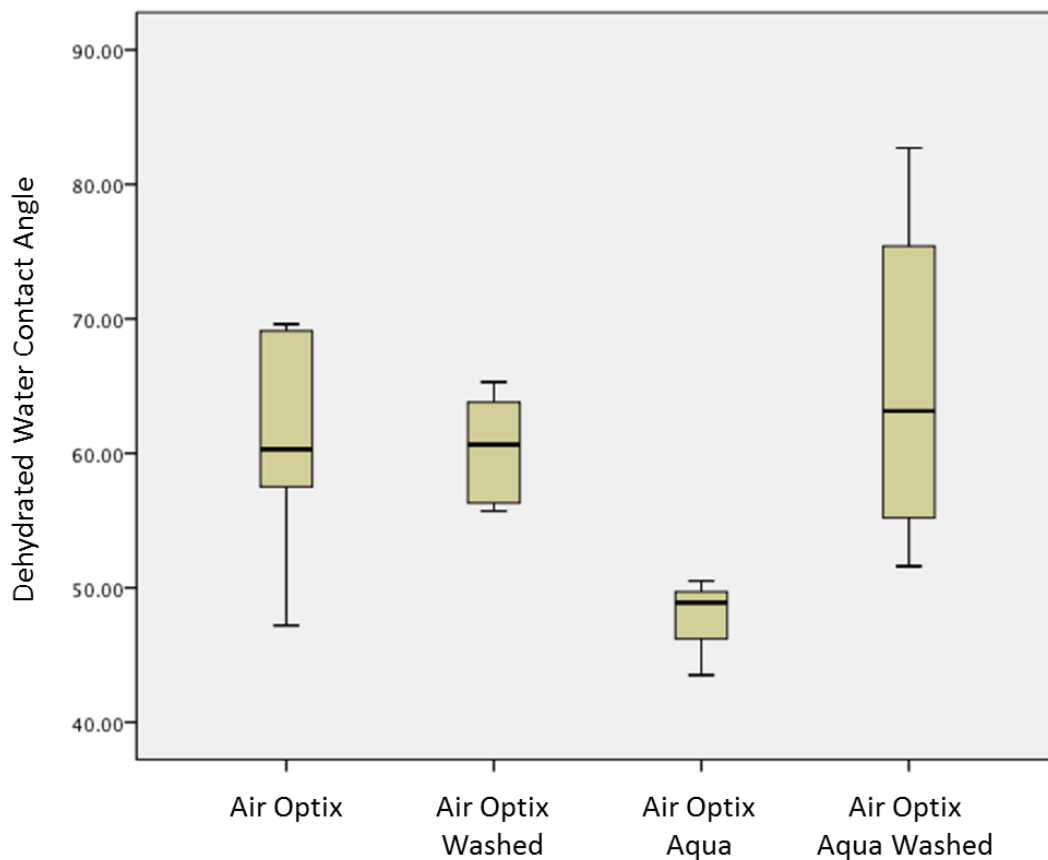


Figure 3.1.3 Dehydrated water contact angles for Air Optix® and Air Optix® Aqua, washed and unwashed (2014).

Statistical analysis was done on the above data (see Figure 3.1.4 and Figure 3.1.5). The Oneway ANOVA level shows a near significance at the 0.07 (0.05 would be considered significant). However, further evaluation using Post Hoc LSD, shows statistical significant (0.01) difference between Air Optix® Aqua and Air Optix® Aqua washed. This means that a briefly washed Air Optix® Aqua lens is significantly different to the lens straight from the packing solution. Additionally, there is a significant difference (0.05) Air Optix® aqua and Air Optix® washed. There is near significant difference between Air Optix® Aqua and Air Optix® at the 0.051 level, this is clearly because of the low contact angle outlier in this particular data set.

► Oneway

ANOVA

ca					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	624.739	3	208.246	2.878	.069
Within Groups	1157.539	16	72.346		
Total	1782.278	19			

Figure 3.1.4 Oneway ANOVA for Air Optix® and Air Optix® Aqua data

Post Hoc Tests

Multiple Comparisons

Dependent Variable: ca
LSD

(I) lenst	(J) lenst	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
ao	aow	.34000	5.15043	.948	-10.5784	11.2584
	aoa	13.10667	6.21165	.051	-.0614	26.2748
	aoaw	-4.46000	5.15043	.399	-15.3784	6.4584
aow	ao	-.34000	5.15043	.948	-11.2584	10.5784
	aoa	12.76667*	6.01441	.050	.0167	25.5166
	aoaw	-4.80000	4.91074	.343	-15.2103	5.6103
aoa	ao	-13.10667	6.21165	.051	-26.2748	.0614
	aow	-12.76667*	6.01441	.050	-25.5166	-.0167
	aoaw	-17.56667*	6.01441	.010	-30.3166	-4.8167
aoaw	ao	4.46000	5.15043	.399	-6.4584	15.3784
	aow	4.80000	4.91074	.343	-5.6103	15.2103
	aoa	17.56667*	6.01441	.010	4.8167	30.3166

*. The mean difference is significant at the 0.05 level.

Figure 3.1.5 Post Hoc Tests for Air Optix® and Air Optix® Aqua data

Figure 3.1.5 shows there is no significant difference between Air Optix®, Air Optix® washed and Air Optix® Aqua washed. The data in Figure 3.1.1-Figure 3.1.5 show that copolymer 845 Aqua additive is not persistent and is removed after a single wash with HPLC water and Air Optix® Aqua in-eye is effectively Air Optix® after several blinks.

Acuvue® 1 Day Moist also has PVP added to the packing solution to increase in-eye comfort. Unlike Air Optix® Aqua, the PVP is more persistent at the Acuvue® 1 Day moist lens; a brief wash does not remove all of the surfactant molecules. This is

because etafilcon A is a negatively charged material and PVP is more attracted to this surface. The wash however appears to remove some surfactant. The water and diiodomethane contact angles have large error bars (see Figure 3.1.1), so the amount of PVP removed in the washing step varies measurement to measurement.

The contact angle data presented for Clariti® materials also have large error bars, especially for the water contact angle values (see Figure 3.1.1). Filcon II 3 (Clariti® material) is the only contact lens material that polymerises large amounts of NVP into the matrix of the contact lens material. The manufacturing process involves a water extraction step but not all of the PVP molecules are fully extracted and subsequently leach from the material during packaging and use. This PVP elution is not entirely disadvantageous and appears to behave in the same way that PVA extraction in producing good initial in-eye wettability as will be shown further on. The PVP in this case is coming from the lens material and not the packing solution. The washing step is unlikely to remove all of the PVP, if a manufacturing extraction step does not. The Clariti® material shows lens to lens variation throughout.

3.2. Surface energy components of dehydrated contact lenses

The purpose of this thesis is to study the surface energy of contact lens materials and surfactant solutions. The surface energy will then be used as a possible indicator for surfactant persistence on the surface of a hydrogel based material. In terms of contact lenses, there are several ways in which the lens material is modified to improve comfort, wettability or coefficient of friction. One way is by attracting hydrophilic molecules to the surface or by eluting hydrophilic molecules from the material matrix, modifying the surface as they emerge. Focus Dailies® elute PVA from the material matrix in a similar way that Clariti® and Clariti® 1 Day contact lenses elute PVP molecules from the surface. Focus Dailies® have controlled gradual release of large PVA molecules to make the lenses more wettable. Clariti® and Clariti® 1 Day however has uncontrolled PVP elution and this is known as residual release. The molecular weights of the PVP molecules being released from Clariti® are of various sizes. Large molecular weight molecules are more favourable because they are less irritating to the

eye. The lower molecular weight molecules can cause more disruption to the cornea as they are able to penetrate the lipid barrier between corneal cells.

In terms of surface chemistry techniques such as sessile drop and friction, the molecular weight of the PVP cannot be distinguished. The Focus Dailies® and Clariti® contact lenses will have measurements that are lubricous and wettable and these properties are both linked to comfort [5]. This highlights that there are many variables in addressing contact lens comfort.

The water and diiodomethane contact angles from the previous section are used to calculate the surface free energy results. The Owens-Wendt equation described in section 0 is used to gain the polar and dispersive surface free energy values.

Here in Figure 3.2.1 the surface free energy is divided into polar (blue) and dispersive (red) components.

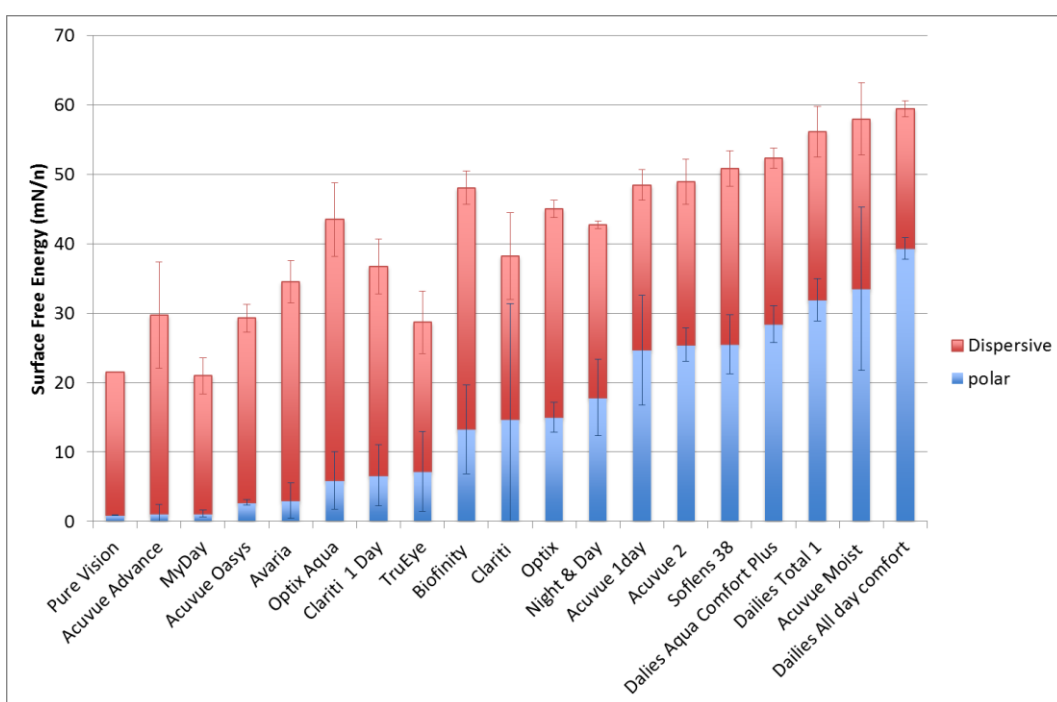


Figure 3.2.1 Polar and dispersive surface free energies of several commercial contact lenses. (The error bars are produced by calculating surface energy values with the highest water contact angle and lowest diiodomethane contact angle and vice versa. The lenses are presented in order of increasing polar component.)

The results here are from lenses that were measured in a dehydrated condition. The different surface energy components can be related to specific in-eye lens behaviour.

For example high polar component values for a surface indicate a more wettable material [47]. The silicone hydrogel materials in Figure 3.2.1 are displaying low polar surface energies. There are a number of reasons why the silicone hydrogel materials may display low polar surface energy. The silicone materials presented here all have relatively low water contents in comparison to the conventional materials. Water has a large polar component and a contact lens with high water content is likely to also have a large polar component (Dailies® lenses). Silicone hydrogel materials contain siloxy macromers. Silicone is very hydrophobic and when it is incorporated into the contact lens material the silicone naturally wants to expose itself at the air interface. The drive for the silicone to get to the surface is increased when the lenses are dehydrated. Silicone hydrogel lenses such as Focus Night and Day and Air Optix®, have a plasma coatings that mask the naturally hydrophobic behaviour of the silicone. This is why Night and Day has a higher polar component than the rest of the silicone hydrogels. Dailies® Total 1 is also classified as a silicone hydrogel contact lens; however it has a hydrogel coating that has a water content of 80%. So for any surface analysis presented here, Dailies® Total 1 behaves in effect as a conventional hydrogel. The conventional hydrogel contact lenses shown in Figure 3.2.1 have the higher polar components. This implies the contact lens surface of a conventional hydrogel still has a great affinity for water, even after dehydration of the lens.

The overall results show separate trends for silicone and conventional hydrogels under dehydrated conditions. The lowest polar fraction values are observed from uncoated silicone hydrogels, followed by the coated or surfactant leaching silicone hydrogels. Then conventional hydrogel lenses have the highest polar fraction values.

The dispersive surface free energy component is dependent on the molecular weight of a material. This is because the dispersive component reflects the induced dipole-dipole interactions created by electrons. As the number of electrons increase, so does the dispersive energy. Table 3.2.1 lists the surface free energy of four dispersive liquids in order of molecular weight.

Table 3.2.1 The surface free energy and chemical formula of several dispersive liquids[122]

Chemical	Surface Tension (mJ/m ²)	Chemical Formula
Hexane	18.7	C ₆ H ₁₄
Octane	21.6	C ₈ H ₁₈
Decane	23.8	C ₁₀ H ₂₂
Tetradecane	26.6	C ₁₄ H ₃₀

The dispersive component values are very similar for all the contact lenses. Contact lens materials consist of similar ‘building block’ molecules. As the dispersive component is dependent molecular weight, it is to be expected that the dispersive values would be within a similar range.

The tear film consists of several layers including a lipid layer. Within the lipid layer there are polar and non-polar lipids (a greater number of the latter).[123] The non-polar (dispersive) lipids are attracted to the dispersive surface energy of the contact lens material. A larger dispersive component leads to more lipid spoliation of the lens surface. This information is useful because contact lens lipid spoliation for fortnightly or monthly replacement lenses can contribute to wearer discomfort and discontinuation of contact lens use.

Figure 3.2.2 shows raw data values for the surface energies; a better illustration is to use the fraction values, as the relative composition is more important.

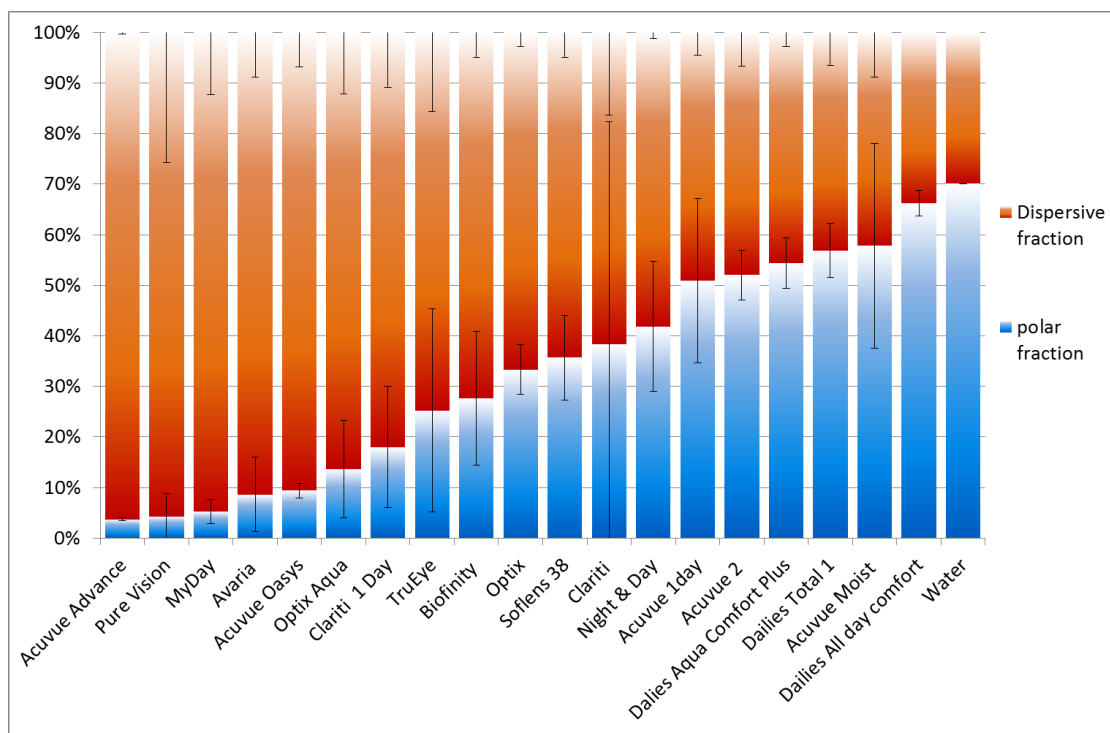


Figure 3.2.2 Polar and Dispersive Fractional surface energies of several commercial contact lenses and water.

The contact lenses in figure are in order of increasing polar fraction. The order of materials in Figure 3.2.1 and Figure 3.2.2 are very similar. This means that in general a high polar surface free energy leads to a high total surface free energy.

The polar fraction of Dailies® All Day Comfort contact (ADC) lenses is very similar to that of water. This is unsurprising, because Dailies® ADC has the lowest water contact angle and has a very wettable surface, even under dehydrated conditions. The variability of the polar fraction for all contact lens materials is greater than the variability of the dispersive fraction. This relates back to points previously made on polar surface energy being more susceptible to contamination (see section 3.1).

The contact lenses with the most variable polar fractions are Acuvue® TruEye®, Clariti® and Acuvue® 1 Day Moist. Both TruEye® and Clariti® have extractables, decanoic acid and PVP respectively. Decanoic acid is a fatty acid with a ten carbon backbone; it is unique when compared with fatty acids with different numbers of carbon atoms. Fatty acids with eight carbons or less are completely soluble in water and those with twelve carbons or more are insoluble in water and form monolayers and insoluble micelles. With its ten carbons, decanoic acid is soluble in water but is also partly hydrophobic.

This means it displays surfactant-like behaviour [124]. Decanoic acid molecules could be present at the surface of TruEye® contact lenses, influencing the wettability of the contact lens surface. This fatty acid is used in the manufacturing process of TruEye® lenses and release from the material is not controlled. If this is the case then the level of decanoic acid influence on the lens surface could be varied lens to lens and could be the reason for increased variability of the polar fraction data.

PVP is able to polymerise into different sized chain lengths. As mentioned in section 3.1, large molecular weight surfactants cause less discomfort to the contact lens wearer. Clariti® contact lenses are polymerised with PVP molecules and the PVP chains post polymerisations are of various sizes. Small molecular weight PVP can disrupt the tear film and cause discomfort. The variation of PVP molecule sizes could be the cause of the Clariti® polar fraction variability. Molecular weight also influences the persistence of molecules at the surface of a contact lens; large molecules are more persistent (see section 6). The PVP release from Clariti® is uncontrolled and any number of large or small molecular weight PVP molecules could be present on the contact lens surface. In this thesis the surface measurement techniques, do not discriminate between molecular weight and any PVP present at the surface will show the contact lens to be more hydrophilic.

Acuvue® 1 Day moist and Acuvue® 1 Day are both made using the same material; although Acuvue® Moist contains an additional wetting agent. The data for Acuvue® 1 Day is less variable than the data for Acuvue® moist, and Acuvue® 1 Day has a slightly lower polar fraction than Acuvue® Moist. This indicates that the 'Moist' additive is influencing the wettability of the lens surface but this influence varies lens to lens.

The manufacturing processes for Acuvue® TruEye® and Clariti® are dominated by water extraction. Both decanoic acid and PVP are water-soluble but the current processes are not removing all of the residuals.

The sessile drop method measures what is at the surface, whether this is the polymerised matrix of the contact lens material as is the case with most of the other materials, or the polymerised matrix of the molecules being released from the contact

lens materials. Variance arises when the molecular release from the surface is uncontrolled and so appears to different extents between batches and lenses.

3.3. The Relationship between contact lens surface properties and bulk properties

It is important to investigate other contact lens properties that can influence wearer comfort. It is also possible that changing one material property could unintentionally change another. Section 1.9 briefly describes the recent evolution of contact lens materials. Conventional hydrogel contact lenses have been available for many years, and from the data presented earlier in this chapter, are (as a group) the most wettable contact lenses. The concern with conventional lenses is their low oxygen permeability (Dk). Contact lenses cover the cornea when they are worn. The cornea acquires oxygen from the air through the tears when the eye is open and from the blood vessels in the eyelid when the eye is closed[125]. Corneal hypoxia (oxygen starvation) has been seen as a cause for corneal swelling growth of limbal blood vessels [126] although recent studies could not link hypoxia to contact lens discomfort[127]. This can cause adverse effects to the health of the eye. Conventional hydrogel lenses transport oxygen through the water molecules in the material. The higher the equilibrium water content (EWC) the greater the oxygen permeability, water has an oxygen permeability of 100 Barrers[53]. A further limitation here is the material durability. If the water content is too high the contact lenses would be delicate and easily damaged. The drive to increase oxygen permeability of contact lenses lead to the manufacture of silicone hydrogels. Silicone rubber has an oxygen permeability of approximately 600 Barrers [128] much greater than water. Silicone hydrogel contact lenses have higher Dk values but silicone is very hydrophobic. The silicone hydrogel equilibrium water content can be increased to improve the wettability of the contact lenses. Since the oxygen permeability of water is ten times less than that of silicone, the addition of more water reduces the overall Dk value of the silicone hydrogel[129]. For both Silicone and conventional hydrogels there needs to be compromise between, EWC, Dk and material durability.

There are other ways to increase the wettability of a contact lens surface without altering the material properties. Contact lens companies try to mask the hydrophobic behaviour of the silicone, either through plasma coating on the surface, surfactants leaching from the material or a hydrogel coating. All of these approaches do influence the wettability of the contact lens surface but to different degrees and persistence.

This section focuses on two bulk material properties, the equilibrium water content and oxygen permeability and their relationship to the material surface free energy. Figure 3.3.1 shows the polar fraction and equilibrium water content for selected silicone hydrogels.

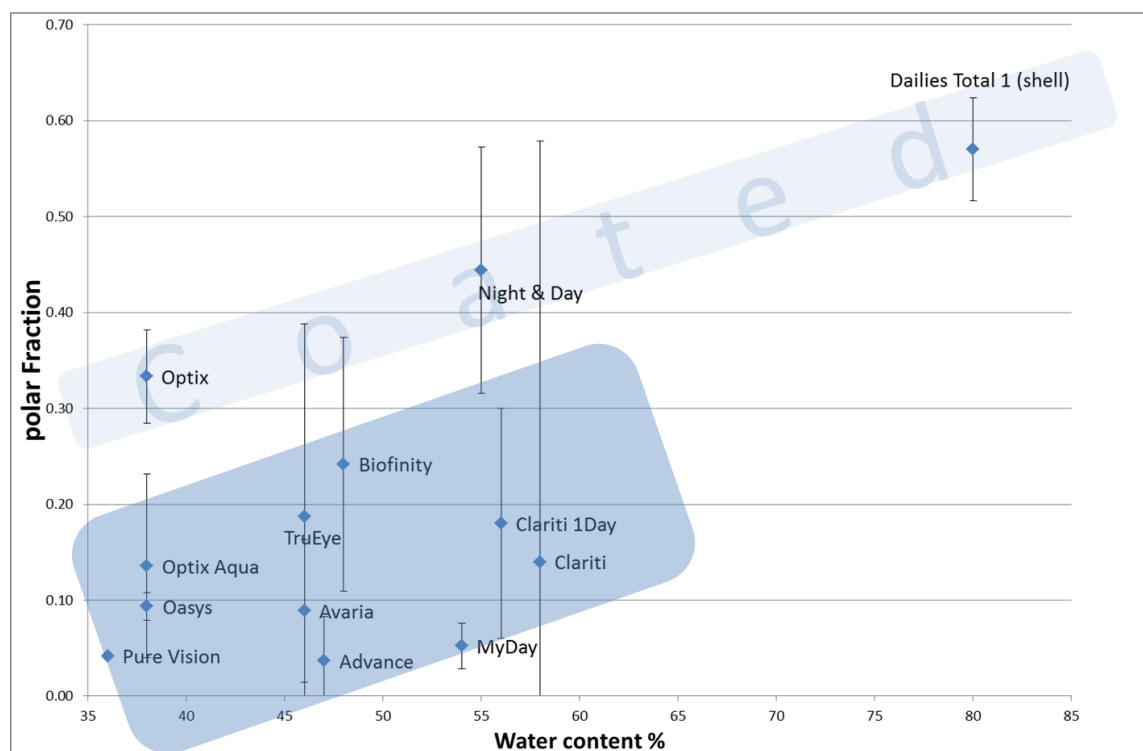


Figure 3.3.1 Equilibrium Water content vs. Polar fraction. Commercially available silicone hydrogels are shown.

It is clear from this data which silicone hydrogel lens surfaces are modified. Air Optix®, Night & Day® and Dailies® Total 1 have higher polar fractions than all of the other silicone hydrogels. Both Air Optix® and Focus Night & Day® are plasma treated. This treatment masks the hydrophobic nature of the silicone in the lens material. Air Optix® Aqua is also plasma treat but the copolymer 845 that is present at the surface displays increased hydrophobic behaviour when the contact lens is dehydrated. Dailies® Total 1

has a conventional hydrogel coating with an 80% EWC and a silicone hydrogel core with only 33% water content. This combination of conventional hydrogel and silicone hydrogel allows for high Dk without the hydrophobic effects of silicone at the lens surface.

Any surface analysis on Dailies® Total 1 should reflect the material properties of the hydrogel coating, and for the data presented in this chapter it does. The other silicone hydrogel contact lenses form a general pattern where the polar fraction increases as the equilibrium water content is increased. The trend follows a gentle incline from Pure Vision® to Clariti® 1day (increasing polar fraction and EWC). Most of the uncoated silicone hydrogels follow this trend.

Biofinity® has a higher polar fraction than would be expected for the material EWC. The oxygen permeability of Biofinity® lenses is also higher than would be expected, see Figure 3.2.2 , this may be because of the composition of the Biofinity® material. *'Biofinity® is made with long chain silicone containing macromers that (according to the manufacturers) allow more efficient oxygen transport so less silicone is needed to give desired permeability' [130]* The unique use of macromers may also attribute to the increased polar fraction of the material.

Figure 3.3.2 shows the polar fraction and equilibrium water content of selected conventional hydrogels.

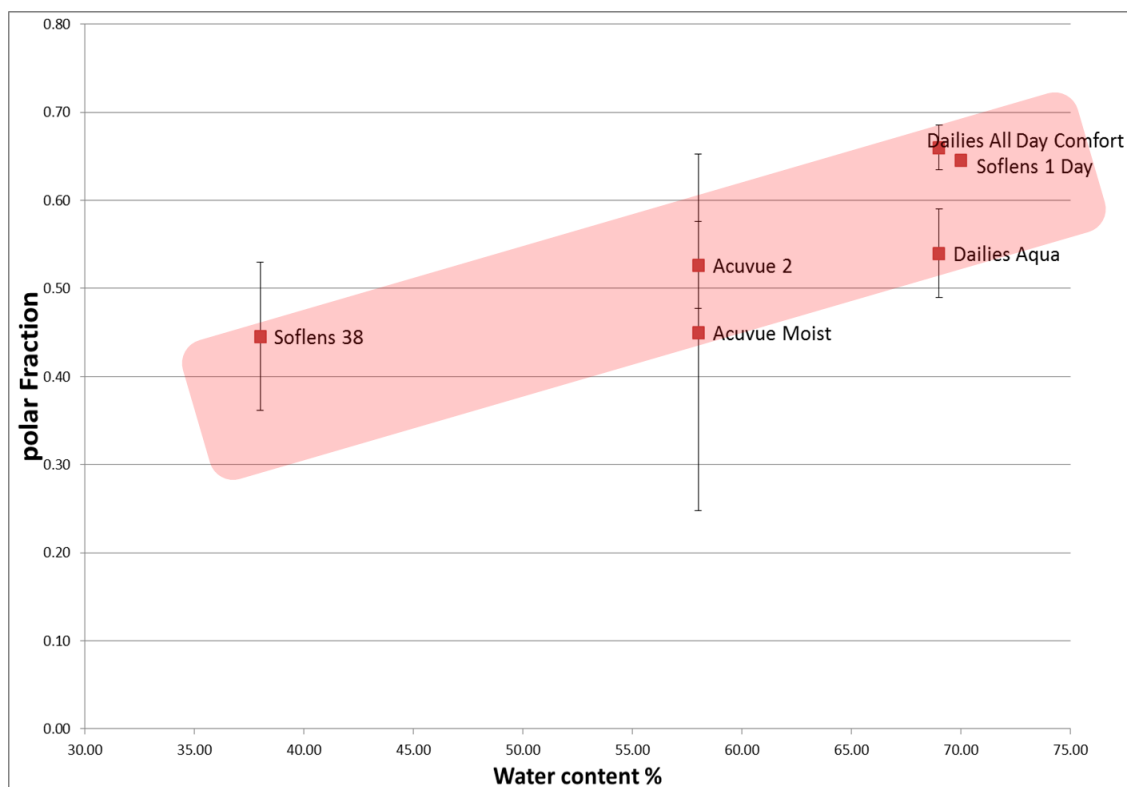


Figure 3.3.2 Equilibrium Water content vs. Polar fraction. Commercially available conventional hydrogels are shown.

The highlighted trend bar is much narrower than the one shown on Figure 3.3.1. This is most likely because the conventional lenses shown here have no surface modification. The surface energy values are of the inherent material properties. The polar component increases as the equilibrium water content increases. Acuvue® moist has a large polar fraction error. This can be attributed to the PVP 'Moist' additive in the contact lens packing solution and is discussed further in section 3.1.

The data in Figure 3.3.3 shows different trends for each lens group.

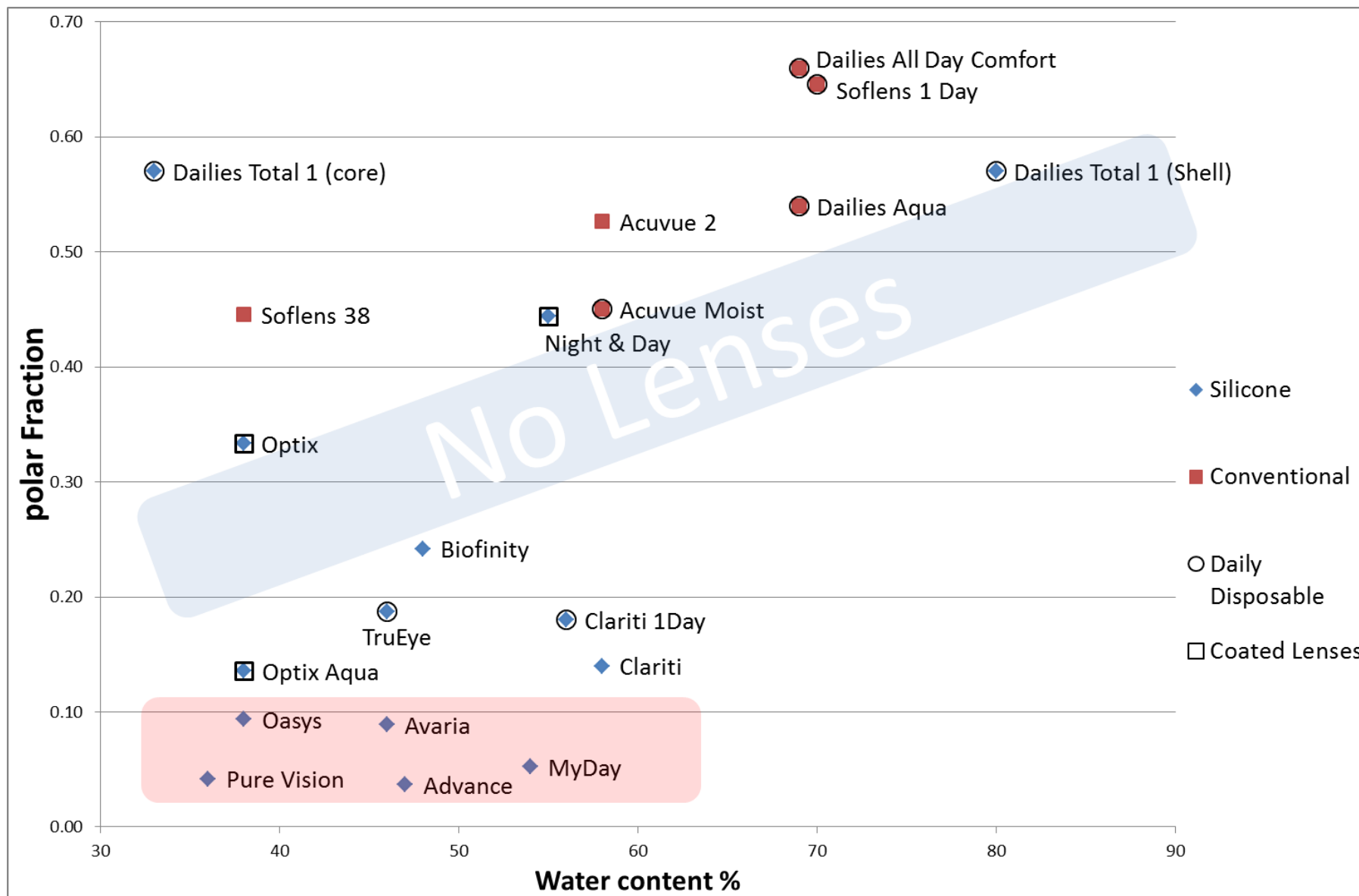


Figure 3.3.3
Equilibrium Water content vs. Polar fraction. Commercially available conventional and silicone hydrogels are shown. Daily disposable materials are circled and coated materials are shown with a square outline.

Table 3.3.1 Tabulated polar fraction data for silicone hydrogel and conventional hydrogel lenses

LENS	Water %	Polar Fraction	SD
Silicone			
<i>Advance</i>	47	0.04	0.046
<i>Oasys</i>	38	0.09	0.014
<i>Optix</i>	38	0.33	0.05
<i>Optix Aqua</i>	38	0.14	0.1
<i>True eye</i>	46	0.19	0.2
<i>Purevision</i>	36	0.04	0.003
<i>Night and Day</i>	55	0.44	0.13
<i>Dailies Total 1 (core)</i>	80	0.57	0.054
<i>Dailies Total 1 (shell)</i>	33	0.57	0.054
<i>Clarity</i>	58	0.14	0.44
<i>Clarit 1 Day</i>	56	0.18	0.12
<i>Biofinity</i>	48	0.24	0.13
<i>Avaira</i>	46	0.09	0.074
<i>MyDay</i>	54	0.05	0.024
Conventional			
<i>Dailies all day comfort</i>	69	0.66	0.025
<i>Dailies aqua comfort plus</i>	69	0.54	0.05
<i>1 Day Acuvue Moist</i>	58	0.45	0.2
<i>Softlens 1 day</i>	70	0.65	
<i>Acuvue 2</i>	58	0.53	0.05
<i>Softlens 38</i>	38	0.45	0.084

Statistical analysis for all of the data presented in Figure 3.3.3 was carried out to highlight any statistically significant behaviour. An Oneway ANOVA is an omnibus test that shows significance (Figure 3.3.4.) The Post Hoc tests show that there are significant differences between silicone hydrogel lenses and conventional hydrogel lenses, silicone hydrogel lenses and coated silicone hydrogel lenses, both significant at the 95% level. The difference between conventional hydrogel lenses and coated lenses is not significant; this further reiterates that coated (silicone hydrogel) contact lenses behave more like conventional hydrogel lenses. The coating successfully masks the hydrophobic nature of the silicone material.

→ Oneway

ANOVA

pf					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.757	2	.879	41.685	.000
Within Groups	1.138	54	.021		
Total	2.895	56			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: pf
LSD

(I) lenstype	(J) lenstype	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
hydro	shydrogel	.35780*	.03921	.000	.2792	.4364
	coated	.13703	.10613	.202	-.0758	.3498
shydrogel	hydro	-.35780*	.03921	.000	-.4364	-.2792
	coated	-.22077*	.10653	.043	-.4343	-.0072
coated	hydro	-.13703	.10613	.202	-.3498	.0758
	shydrogel	.22077*	.10653	.043	.0072	.4343

*. The mean difference is significant at the 0.05 level.

Figure 3.3.4 Oneway ANOVA of polar fraction and lens type data and Post Hoc tests

However, the category of lens type is influenced by water content. In general silicone hydrogels lenses have lower water contents than conventional hydrogel lenses and, in general low water content materials present a low polar surface. Further statistical analysis was carried out to show the significance of each variable (please see Appendix 9.4). The statistical significance between lens type and polar fraction was still calculated as significant.

The conventional materials all have a high polar fraction; in general they also have higher water content. The polar fraction increases as the water content increases. The surface of Dailies® Total 1 falls suitably into this trend. That is expected as the surface of Dailies® Total 1 has a hydrogel coating.

Biofinity® lenses have the highest polar fraction of the uncoated silicone hydrogel materials. CooperVision, who produce Biofinity® also produce Avaira® and MyDay®. Both these lenses have a much lower polar fraction, even though the water content

for MyDay® is higher than that for Biofinity®. One explanation for this difference is the polymerisation process. Biofinity® is cured through UV polymerisation, this process occurs in hydrated conditions and at ambient temperatures. The heating effects are minimal and reaction times are relatively short.[131] UV polymerisation is not suitable in all cases, for example if lens material contains UV blockers. The thermal method is a more established process, polymerisation occurs over a longer period of time at high temperatures. After thermal polymerisation the material needs to be hydrated.

When silicone hydrogel materials are dehydrated the silicone molecules rotate, present themselves at the surface and mask the hydrophilic molecules. Biofinity® is characterised by the presence of siloxy macromers only (no TRIS molecules) and Biofinity® siloxy macromers have embedded peg units incorporated into the chain. This is so that the siloxy groups cannot readily separate themselves from the hydrophilic PEG groups.

The group of lens materials highlighted in the red band have a range of water contents. These materials are compositionally hydrophobic and the polar fractions will be low regardless of their water content.

From the data shown in Figure 3.3.3, silicone hydrogel lenses do not form any obvious pattern or any clear line in relation to water content. In contrast, conventional hydrogel lenses show that an increase in water content leads to a higher polar fraction. This is unsurprising as water is highly polar, it would be expected that a material with increased water content would be increasingly polar. The coated silicone hydrogel lenses (Focus Night and Day and Air Optix®) are easy to notice as they fall more in line with the conventional materials. This is the manufacturer's intention as silicone materials have higher oxygen permeability but these lenses have conventional hydrogel surface behaviour.

Dailies® Total 1 falls away from the other lenses on the graph. The hydrogel coating has 80% water content, but the whole lens only has 33% water content. The silicone in the core is effectively masked by the hydrogel layer and the polar surface energy and wettability have been increased.

Night and day and Optix® are coated and behave differently to the silicone hydrogel general trend. Optix® aqua falls lower due to the hydrophobic nature of CP845 under dehydrated condition.

Figure 3.3.5 shows data previously presented to illustrate how oxygen permeability of a contact lens material is altered by water content and silicone content.

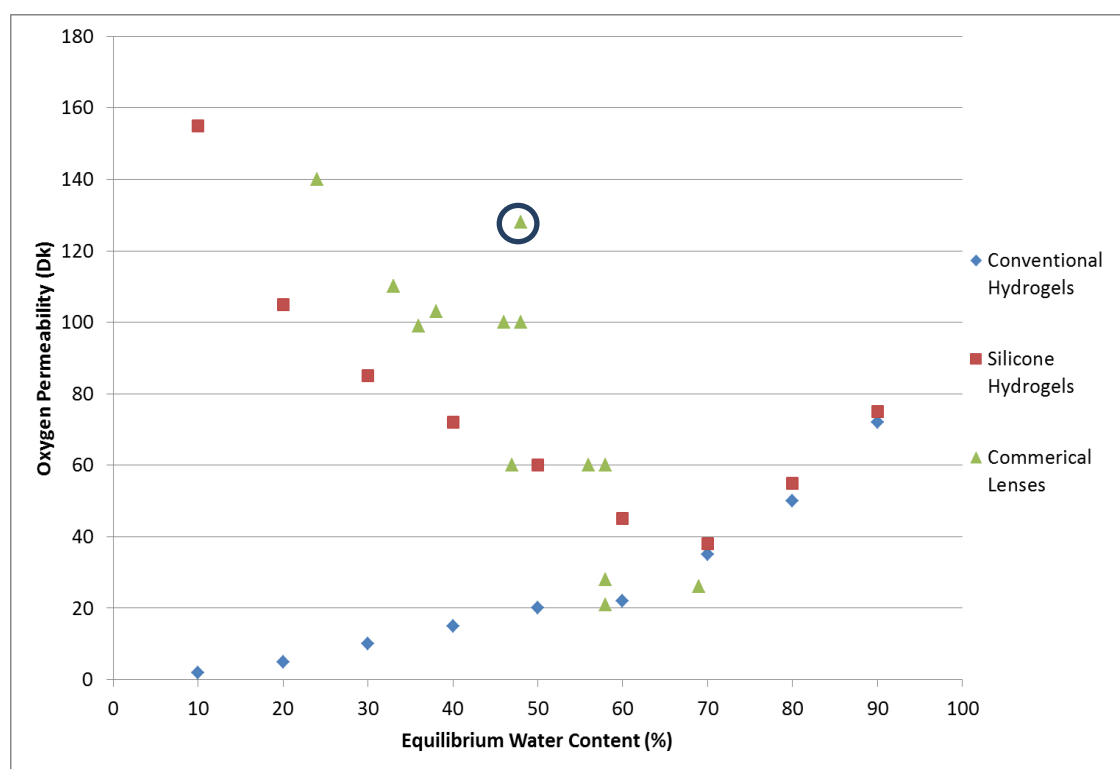


Figure 3.3.5 Equilibrium water content vs oxygen permeability (Dk). Comparing conventional hydrogel, silicone hydrogel and commercially available materials [132]
The circled point is Biofinity®, this material has been shown to behave differently to what would be expected for its material properties.

From the literature, it is known that oxygen permeability of a conventional hydrogel increases as the equilibrium water content increases. For silicone hydrogel materials the oxygen permeability decreases as the equilibrium water content increases. The above graph also shows the commercial data for many of the contact lenses presented in this chapter. Half sit within the idealised values for conventional and silicone hydrogel materials. The other half has higher Dk values. Tighe[56] states that for materials with water contents below 50 per cent, the oxygen permeability is dependent on the precise composition of the non-aqueous part of the structure. This is not defined in the figure and can be different for each material. This means that it is

possible for silicone hydrogel materials to have higher and lower permeability than those shown on Figure 3.3.5. Biofinity®, which is circled on the graph, has a much higher Dk than would be expected. As previously explained, the reason for this is material composition.

Throughout this chapter error bars have been presented with most of the data. The surface investigation methodologies used can show a large range of results because they are influenced by many variables including probe solution contamination and droplet analysis. There have been on-going contact angle experiments for most of the materials presented here. This has allowed for contact angle comparisons to be made over time. Two of the lenses that have the greatest variability are Acuvue® TruEye® and Clariti®.

To investigate lens surface changes over time Figure 3.3.6 shows the polar fraction of TruEye® and Clariti® from a 2009 batch and a 2011 batch. In 2009 Sauflon™ issued a batch of lenses in line with the start of the PhD, they then issued an additional batch approximately three years later. This then allows for any changes taking place over time (either as a result of PVP leaching from the lens, or process differences implemented by Sauflon®) to be noted.

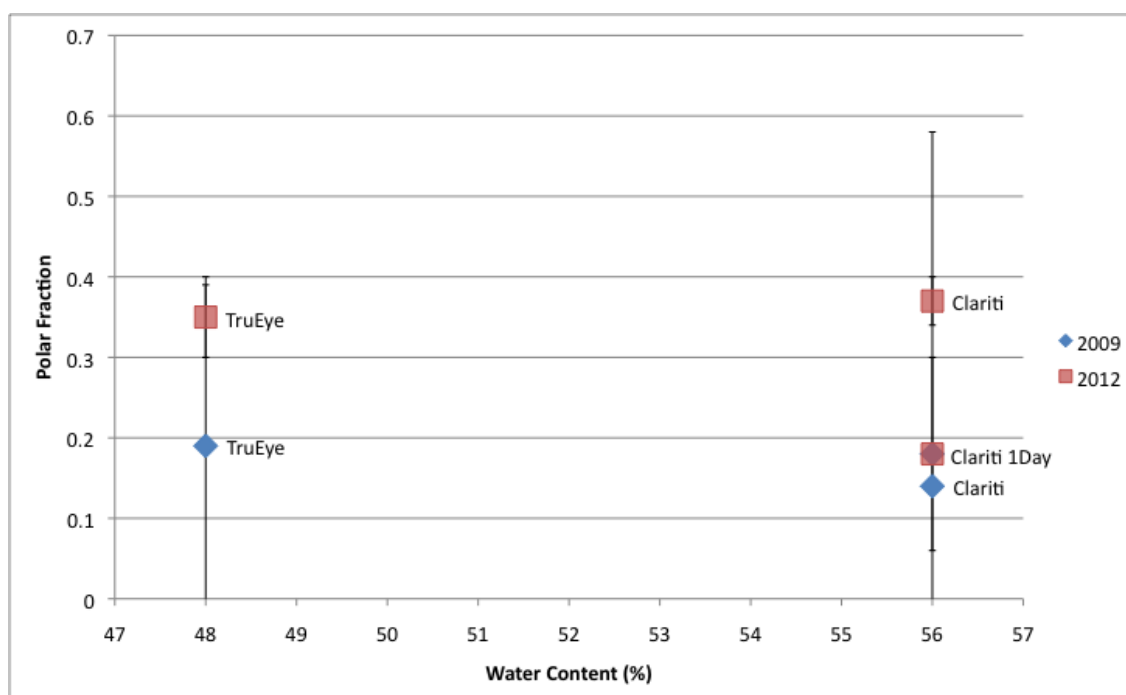


Figure 3.3.6 Polar fraction vs. Equilibrium water content for Acuvue® TruEye® and Clariti® contact lenses. Comparison of data from 2009 and 2012

The contact lens data from 2009 is of a new lens and the data from 2012 is of a lens that is 3 years older. Both TruEye® and Clariti® have different polar fractions for each date and seem to become more polar over time. The increased polar fraction could be because of any residuals present at the surface, decanoic acid for TruEye® and residual PVP for Clariti®.

Previous assessment of the Clariti® material has shown substantial variability in contact angle and surface free energy values, and as previously discussed this could just be attributed to lens to lens variation. There are also differences between Clariti® and Clariti® 1Day. The material for both lenses is Filcon II 3 and the water content is also the same for both lenses. The differences between the two lenses could then be a consequence of assumed process differences. It is also of interest that in 2009, Sauflon® the company that manufacture Clariti® and Clariti® 1 Day had not FDA approval, and were able to change the lens material without being required to inform them or the general public.

Daily wear contact lens materials need to be less expensive to manufacture to be cost effective. Clariti® 1 Day could be leaching more PVP as a result of a shorter

manufacturing process. This could also be a reason why Clariti® 1 Day shows almost no difference between 2009 and 2012. For commercial reasons it is normally the case that daily disposable lenses have faster and less costly production processes than monthly frequently replacement lenses. Almost inevitably this means a reduction in extraction time or the overall effectiveness of the extraction process. If this is the case with Clariti® and Clariti® 1 Day, then Clariti® 1 Day will have more residual PVP in the lens matrix than Clariti®. The PVP leaching from Clariti® 1 Day could already have reached its limit by the time it leaves the manufacturer in the blister packs. Whereas Clariti® may take a longer period of time to leach the same amount of PVP as Clariti® 1 Day. This would lead to differences between the 2009 and 2012 contact lens surfaces. All of the differences for Clariti® materials however, can still be a result of the variability of the material. The polar and dispersive fraction error bars nearly meet and a range of values can be seen for Clariti® and date could be no factor at all.

In regards to TruEye®, there is decanoic acid leaching from the surface of narafilcon A (TruEye®). In Japan narafilcon A was causing wearer discomfort and the material was withdrawn.[133] Narafilcon B was then released in Japan only. This new material had reduced levels of leaching decanoic acid. To reduce the leaching additional extraction was implemented. This extension of the manufacturing process would naturally increase production costs (currently narafilcon B is not being produced[134]). The polar fraction values are different between 2009 and 2012 and this could be because of the decanoic acid leaching over time[135].

3.4. The Coefficient of friction of hydrated contact lens materials

Contact angle data is used in this thesis to calculate the surface free energy (section 3.2). A low water contact angle is displayed by a wettable material. In terms of contact lenses, a wettable material and low water contact angle are necessary for a lubricious surface. The lubricity of a surface is related to the coefficient of friction and stick-slip behaviour of a contact lens.

As previously stated, it is conventional to study hydrated contact lenses and for the friction measurements the contact lens materials were hydrated. This section of the thesis is concerned with the surface energy of a contact lens in order to assess the

material/surfactant hydrophobic and hydrophilic interactions in an aqueous environment. Work by Tanaka [136] and Lee [137] highlight a correlation between coefficient of friction and critical surface tension of polymers where polar interactions are not present. Lee also explains that surface energy relates to the adhesion component of friction and not the sliding friction, the surface energy of the lubrication is important and the elastic properties also contribute [137]. (Surface tension and surface free energy are essentially the same property. Surface tension is usually used to describe the surface free energy of a liquid and surface free energy is used to describe the equivalent characteristics of a solid.) However the correlation observed was in the absence of polar interactions. (Tanaka used hydrophobic polymers with mainly dispersive surface free energies). An equivalent correlation may not be found with the systems studies here as all the materials used have significant polar surface energy contributions.

The calculated surface free energy values are used in this section with the coefficient of friction measurements. The friction traces presented in this chapter are of hydrated daily disposable silicone hydrogel and conventional hydrogel contact lenses.

As mentioned in the previous paragraph, when the solid mechanical properties are similar, the surface free energy and coefficient of friction values may be comparable. However, they may not show any direct relationship as there are polar components present in contact lens materials. The surface free energy and contact angles are also measured under dehydrated conditions. Other variables also complicate the coefficient of friction, such as the modulus of the materials and lubrication. The firmer contact lens materials have higher elastic modulus values and this usually leads to a lower coefficient of friction [138].

The mechanisms put in place to improve the lubricity of a contact lens are designed to reduce the COF not necessarily the polar surface energy and wettability. Lens modifications are an additional variable, Focus Dailies® lenses intentionally release PVA molecules to improve lubricity and Clariti® 1 Day unintentionally leaches PVP, this also affects lubricity.

Figure 3.4.1 shows the average friction traces for several daily disposable contact lenses. All measurements were repeated in triplicate.

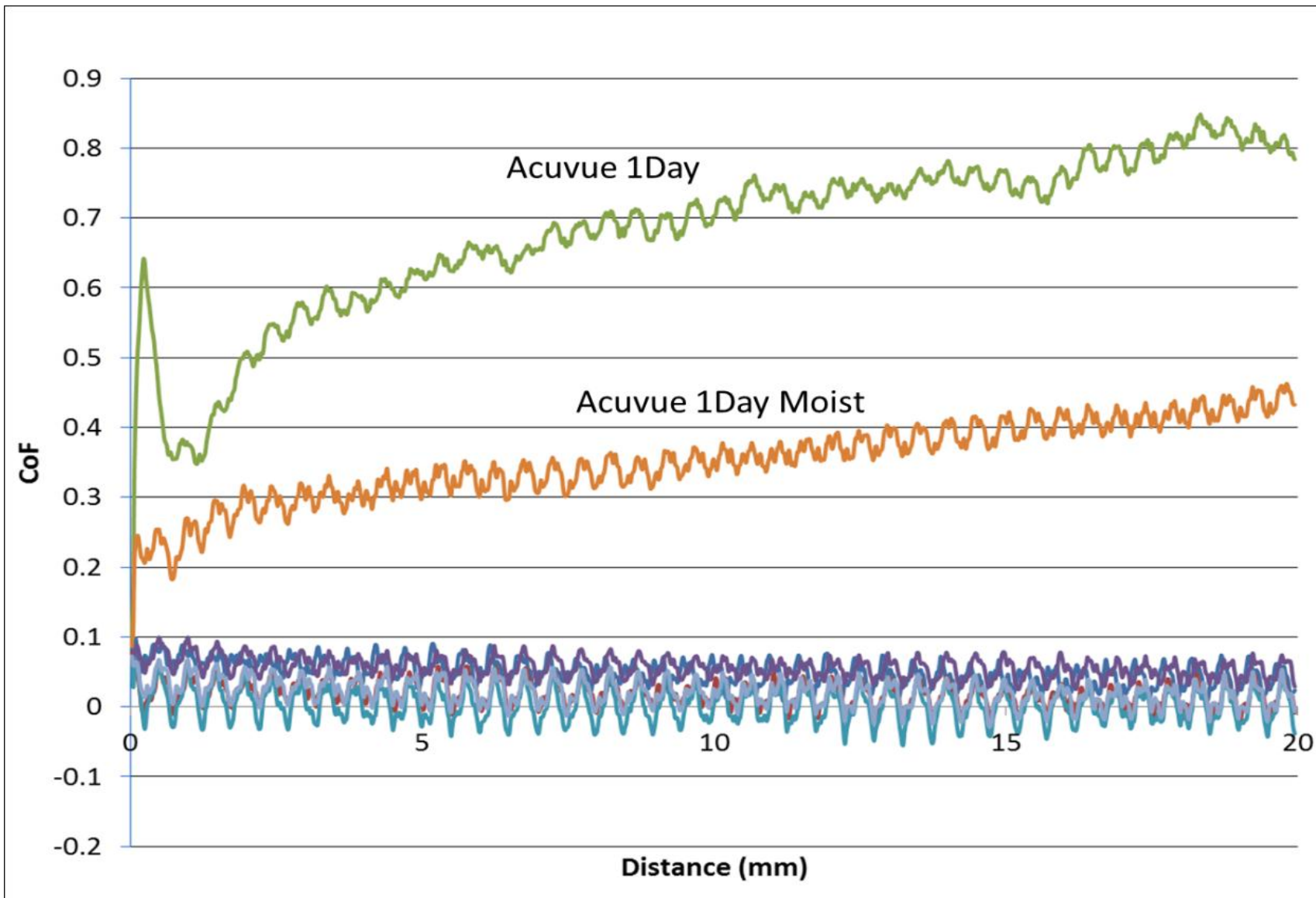


Figure 3.4.1
Coefficient of friction traces from the modified nano scratch tester (CSM Instruments, Peseux, Switzerland) of daily disposable commercial lenses. Mean data from 10 passes at 30mN load and 30mm/min velocity.

From the graph it is clear to see that Acuvue® 1 Day and Acuvue® 1 Day moist have much higher frictional behaviour than the other contact lenses. These high friction traces could be attributed to the low modulus value of etafilcon A (the USAN name for the Acuvue® 1 Day and Acuvue® 1 Day Moist material). Softer materials can show higher frictional behaviour due to their elastic properties. If the modulus values for contact lenses are very different from each other they are not directly comparable. This point highlights again how many factors there are in contact lens wearer comfort. A soft lens is more able to mould itself to the shape of the cornea and this would be seen as an improvement in comfort. However softer materials have higher frictional values and friction behaviour is also seen as an indication of contact lens comfort.

From the graph there is a clear difference between Acuvue® 1 Day and Acuvue® 1 Day Moist. Both contact lenses are made using the same material (etafilcon A) and have the same water content. The only difference between the two is that the Moist lenses have a wetting additive. This addition to lens improves the friction from 0.4-0.8 to 0.2-0.45, approximately half. The other lenses on the graph have similar friction traces at this scale.

An Oneway ANOVA for lens type shows overall significance at the 99% level. A Post Hoc test (LSD-Least Significant Difference) confirms significant differences between Acuvue® 1 Day lenses and all other lens types at the 99.9% level. Likewise, for Acuvue 1 Day® Moist lenses.

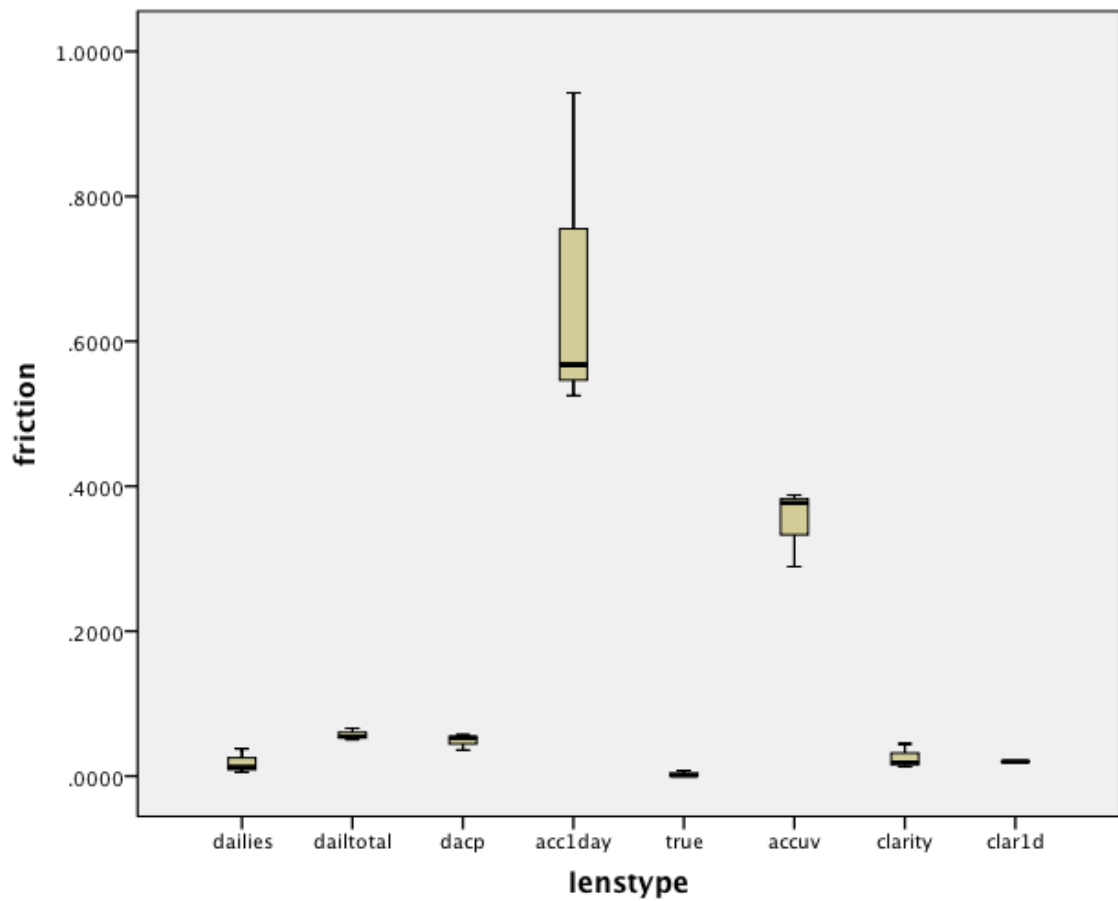


Figure 3.4.2 Box plot from statistical analysis carried out using SPSS software

Figure 3.4.3 below shows the same data as Figure 3.4.1 on a greater scale. This scale shows the friction trace the stick-slip patterns for each lens.

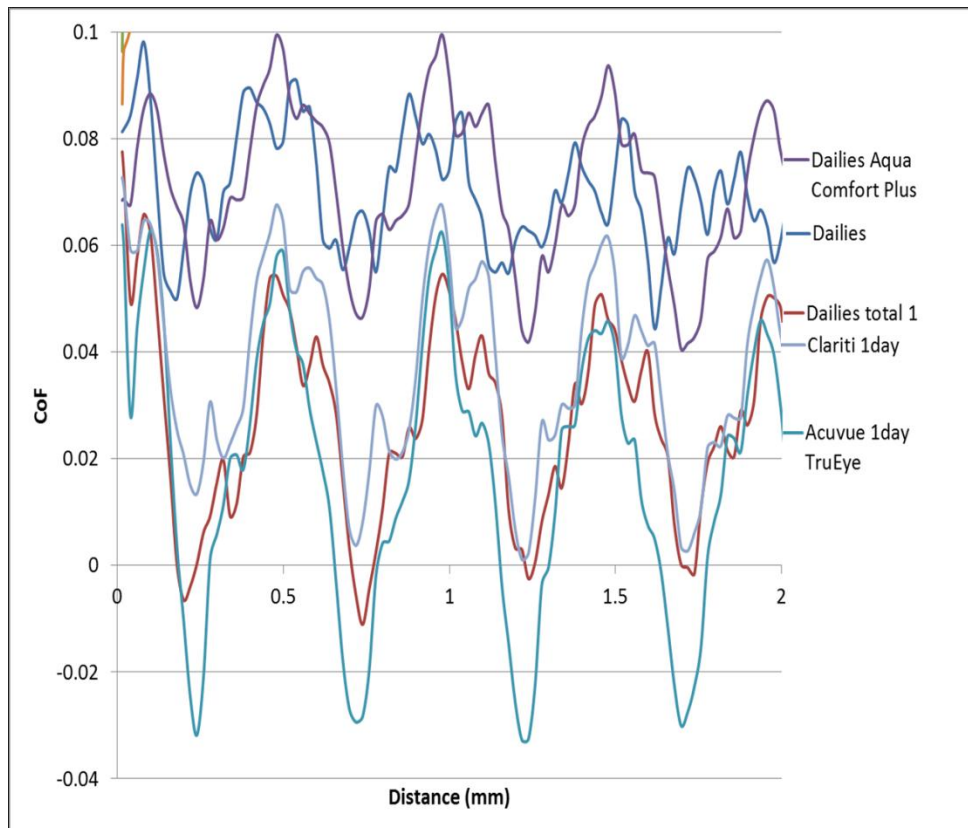


Figure 3.4.3 An increased scale of Figure 3.4.1 to highlight differences between the other lenses

Focus Dailies® and Dailies® Aqua Comfort Plus have very similar patterns and coefficient of friction values, they are both made from the same hydrogel material (nelfilcon A) but Dailies® Aqua Comfort Plus has additional PVA. All Dailies® materials behave similarly. Dailies® Total 1 has a lower coefficient of friction but the stick slip value is larger than the other Dailies® materials. The hydrogel coating on Dailies® Total 1 is has a very high water content in comparison the other hydrogel lenses (Dailies® and Dailies® Aqua Comfort Plus). The modulus value is slightly lower for Dailies® Total 1 and this could attribute to the higher stick-slip. The modulus however is given for the whole material and not for the core and shell separately. Clariti® 1 Day and Acuvue® TruEye® also have similar coefficient of friction values and trace patterns. These lenses are made by different manufacturers and with different materials but they are similar in the way they leach surfactants from the material. This leaching could be affecting the lubrication at the surface of each lens. The stick-slip behaviour is higher for Acuvue® TruEye®. Section 2.8.1 explains the importance of stick-slip and how a lower stick-slip value is another indication of increased comfort.

There is a distinction between the materials. The silicone hydrogel lenses have lower friction than the conventional lenses see Table 3.4.1. The silicone hydrogel lenses also have a higher stick slip value.

Table 3.4.1 Daily Disposables friction Data

Contact Lens	Dailies	Dailies (ACP)	Dailies Total 1	Clariti 1Day	Acuvue 1Day	Acuvue 1Day Moist	Acuvue TruEye
CoF	0.0497	0.0571	0.0187	0.0202	0.6786	0.3513	0.0029
SS	5.7915	5.2394	6.0571	6.6916	7.3997	7.1792	7.7392

Figure 3.4.3 shows the friction traces of 5 daily wear contact lenses with modulus values between (0.5 and 0.7), Acuvue® 1 Day and 1 Day Moist have been omitted as their modulus value is much lower than the other materials and not comparable. Lenses with low modulus values tend to have high frictional behaviour.

From the data presented in this chapter Clariti® and Clariti® 1 Day (Falcon II 3) contact lenses have the greatest range of results, with differences appearing lens to lens. This could be a result of the PVP that is leaching from the lenses. As discussed earlier on in this thesis, the presence of PVP at the surface will increase the lens wettability. However it is not possible to detect PVP through surface tension methodologies such as Du Noüy ring because PVP is not surface active. Additionally PVP can form into a range of different molecular weights, low molecular weight PVP can disrupt the tear film and cause the lipid layer to break up. Through the methodologies used here, there is no way of knowing the PVP molecular weights present at the surface of the lens. The friction data will show and increase in lubricity but the effect on the tear film may cause discomfort.

The fricto-mechanical properties of a material are also very important as these relate to the dynamic behaviour of the contact lens. Increased lens wettability and lubricity will reduce the coefficient of friction. Lubricated lenses show hydrodynamic/aqueous frictional behaviour. While this lubricated water layer persists, the material will show a low coefficient of friction. Over time the lubricated layer may reduce or evaporate completely; boundary layer friction is then observed; with much higher coefficient of friction.

Here in Figure 3.4.4 the modulus is compared to the stick slip value.

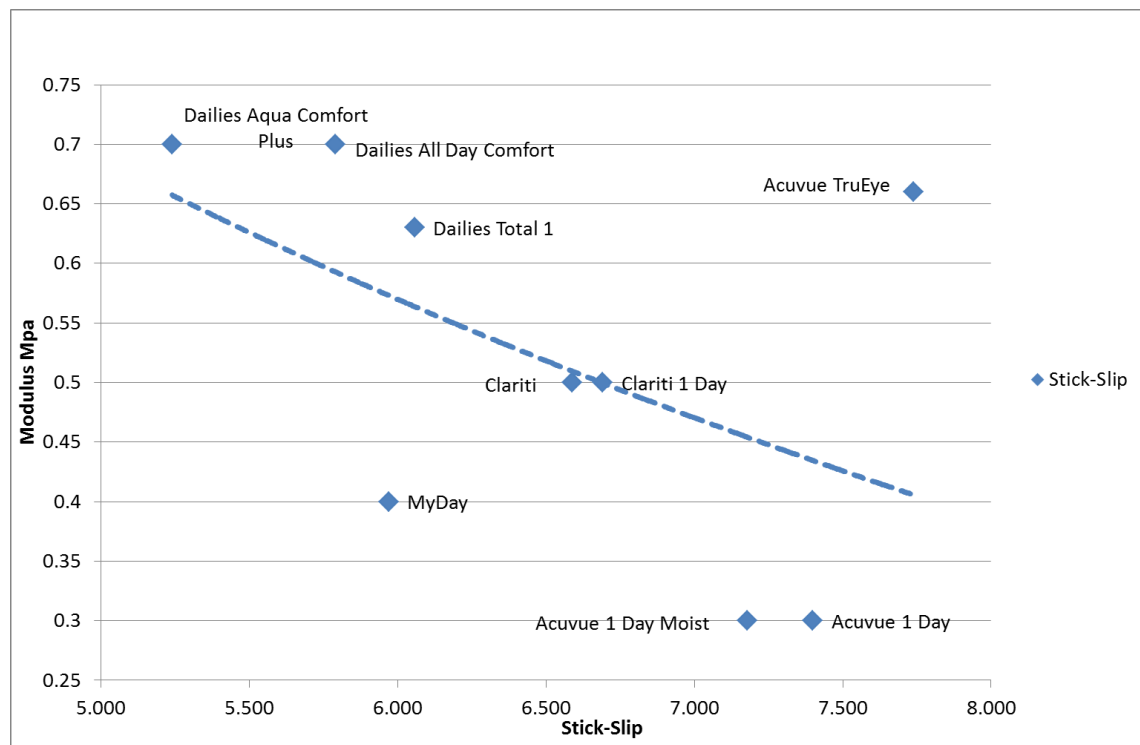


Figure 3.4.4 Modulus values of several commercially available contact lenses in relation to their measured stick-slip value

Both stick-slip and coefficient of friction rise as the modulus value decreases. The moist additive positively affects the stick-slip and Coefficient of friction and so should make the lens more lubricious during wear. TruEye® behaves furthest from the trend when it comes to its stick-slip. All the Acuvue® lenses have the higher stick slip values, regardless of modulus value.

3.5. The static surface tension of contact lens packing solutions

The data presented in Figure 3.5.1 shows the static surface tension results of commercially available contact lens packing solutions.

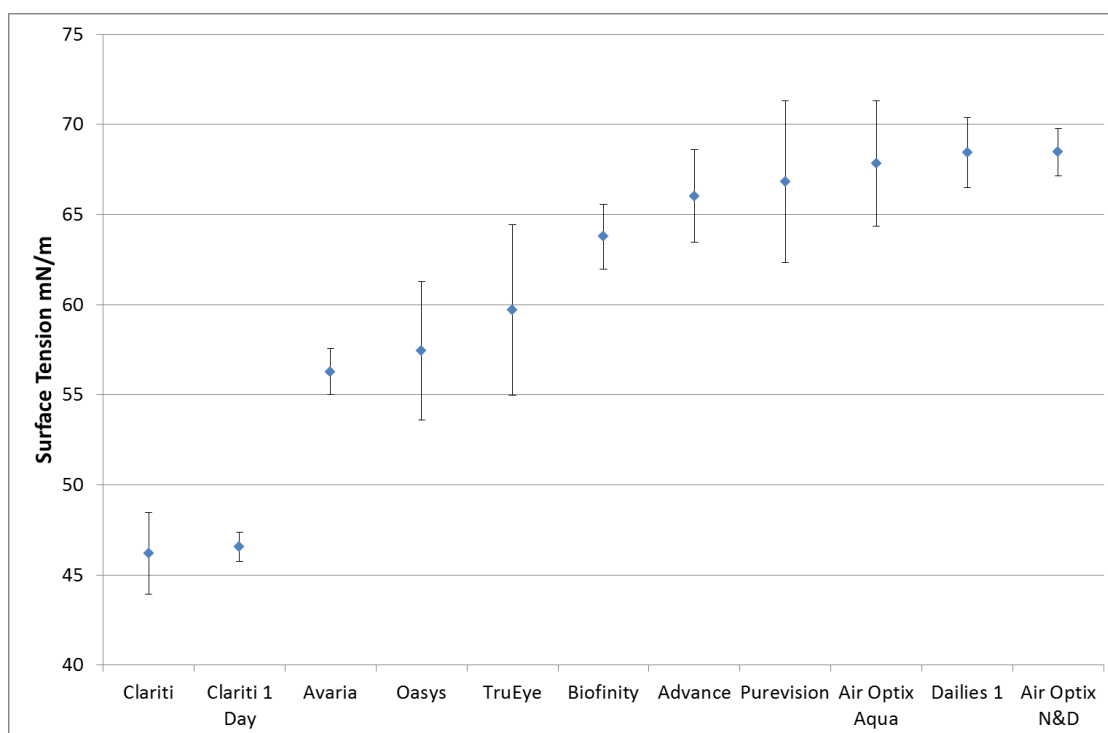


Figure 3.5.1 Surface tension of commercially available packing solutions in ascending order.

The packing solutions correspond to the contact lenses in the previous figures. The mini du Noüy ring (KRÜSS GmbH, Hamburg, Germany) technique was used to measure the blister packing solutions, as there is approximately only 500µl of liquid in each pack. All measurements were repeated in triplicate.

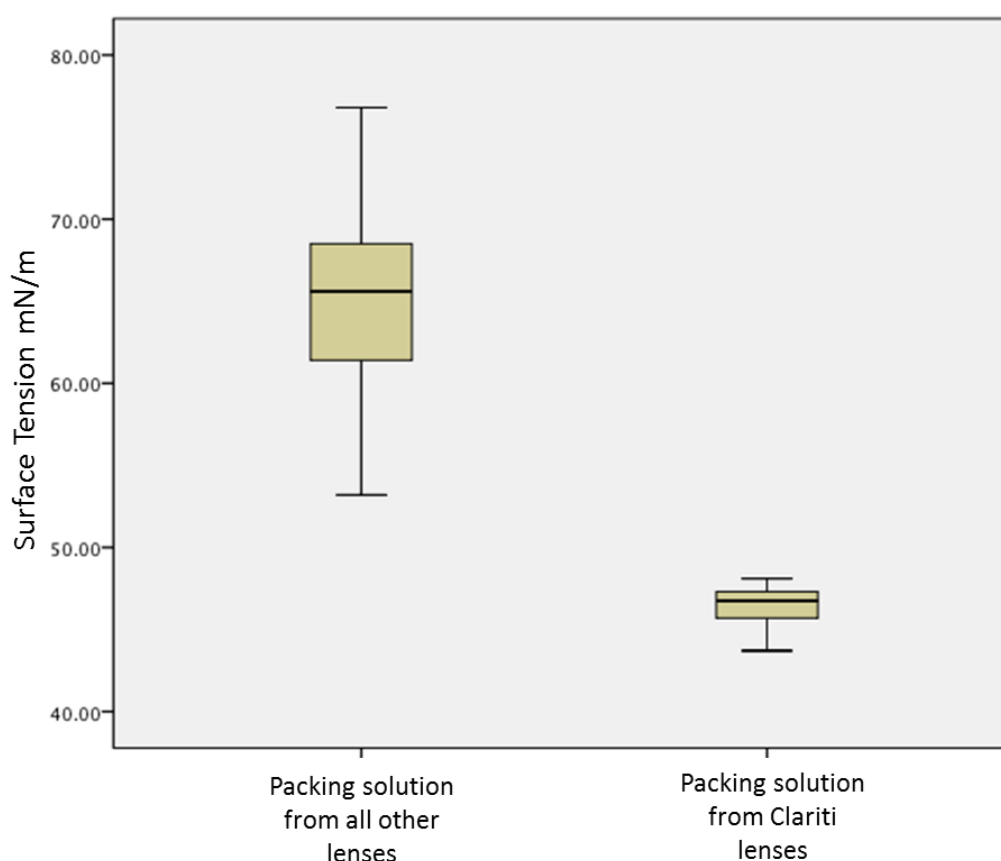


Figure 3.5.2 Box Plot of packing solution surface tension values. Clariti® packing solution against all other contact lens packing solutions.

A Students T-test was used to show statistical significance between the surface tension of Clariti® packing solution and the packing solution from all the other contact lenses tested. The mean surface tension value for Clariti® packing solution is 48mN/m and the mean value for all of the other packing solutions is 62mN/m. This is nearly a 25% reduction ($\frac{62-(48)}{\sqrt{62}} = 0.23$) see Figure 3.5.2.

Figure 3.5.1 shows there is more surfactant in Clariti® packing solution than any other lens; this adds another possible variable to the sessile drop measurements and could explain the large errors bars shown in Figure 3.1.1. There is a significant difference (see Figure 3.5.2) between the surface tension of Clariti® and Clariti® 1 day packing solutions and the surface tension for all the other packing solutions. The surfactant present in the solution is remaining at the surface on the lens, even after a wash step. The presence of surfactant in the packing solution and PVP leaching from the lens

material is making the lens more lubricous and producing a low coefficient of friction. The interaction between PVP and a surfactant is complex and leads to subsequent investigation, which is beyond the scope of this thesis.

3.6. Discussion and Conclusion

The conventional approach to contact lens characterisation occurs under hydrated conditions. However, the results presented in this chapter are obtained through the analysis of dehydrated contact lens materials. There are several material properties that are seen to influence contact lens comfort. The data here shows how materials property measurements can conflict and how improved in vitro behaviour for one property does not always translate into improved in vitro behaviour for the whole lens.

The surface properties of a contact lens influence wearer comfort. When lenses are placed into the eye they are coated by the tears. The tear film consists of hydrophilic (polar) and lipophilic (dispersive) components, it is therefore important to investigate a lens surface in terms of polar and dispersive surface energies. The use of two probe liquids in contact angle analysis allows for these surface energies to be calculated. Water is the usual probe solution to measure contact angles of biomaterials as the body is made up of mainly water and a lipid substitute (diiodomethane) as an additional probe solution adds significant insight into material interaction in a biological environment. In addition to the surface energy the polar fraction of a lens surface can also be calculated. The polar fraction highlights which contact lens surface behave most and least like water. In general contact lenses with low polar fractions are more inclined to have high lipid spoliation[62]. Lipid spoliation can cause wearer discomfort and is of particular importance when a lens is intended for anything other than daily disposable wear.

These data also reveals the variability of several contact lens materials, especially Clariti®. In regards to its water contact angle measurement, the range of values for Clariti® is nearly 20°. The variability of Clariti® can be partially explained by the data presented in Figure 3.3.6 and Figure 3.5.1 the variance with Clariti® could possibly be explained. Figure 3.3.6. shows that the polar fraction for Clariti® monthly changes

from 0.11 to 0.38 over 3 years. This indicates that the surface of Clariti® is unstable and deteriorates in the lens blister pack over time. Clariti® 1 day lenses are less affected by the time lapse. It is known that PVP is present in the lens matrix and the packing solution. The molecules could have eluted in their own time to the surface of the contact lens, creating a more polar surface. As the packing solutions could be an additional variable, the surface tension of the packing solution from all blister packs was measured. Clariti® and Clariti® 1 Day have the lowest surface tension values by almost 10mN/m. The surfactant concentration must be higher than in other packing solutions and would attribute to an increase in polar surface energy and could be a factor in the material variability. (The surface tension of 'in process' packing solution was also measured and the value was within the same error bars as the data presented for Clariti® and Clariti® 1 day).

Surface deterioration also effects the measurement from Acuvue® TruEye®, although the differences are not as marked as the data from Clariti® monthly. The packing solution surface tension falls into a similar range to most of the other packing solutions and so this is less likely to be the cause of any differences. In 2010 Johnson&Johnson™ recalled several TruEye® contact lenses[139] due to decanoic acid leaching from the lens material[135]. Over time in the blister pack the decanoic acid could present itself at the surface of the material and as the acid has surfactant like behaviour it could affect the polar fraction value and cause variation over time.

Several surface measurement techniques are presented in this chapter, including the coefficient of friction. Frictional data is independent of the other data acquired from surface investigation such as surface free energy. This is because of the polar surface energy present in all of the materials presented here. There are several variables that affect the frictional values, for example modulus and lubricity. Materials with low modulus values show higher friction traces and even more so with the stick-slip behaviour. The stick-slip data points in Figure 3.4.4 form a near linear correlation with the exception of Acuvue® TruEye®, which has the highest stick-slip value. The overall frictional behaviour however, is similar to the Dailies® group of lenses.

The surface tension of the blister packing solutions was measured to investigate variations with Clariti® lenses. For all the contact lenses presented in this chapter ranges from approximately 45-68 mN/m. The packing solution from Clariti® and Clariti® 1 Day contact lenses was the lowest of all the values by 10mN/m. This indicates increased amounts of surfactant are present in the packing solution, it is also known that Clariti® materials contain and elute PVP. PVP has shown to influence surfactant behaviour (see Figure 6.2.1.3) and this could affect contact angle and friction data.

Chapter Four

Surface tension behaviour
and critical micelle
concentrations of
Surfactant and Multi-
Purpose solutions

4. Surface tension behaviour and critical micelle concentrations of Surfactant and Multi-Purpose solutions

There is considerable interest in the role of surfactants in multi-purpose solutions (MPS) both in terms of their cleaning (lipid removal) and their potential ability to improve the comfort of contact lenses by surfactant adsorption onto the lens surface.

There are two interfaces that are important for this work; air/water and contact lens/water. As Chapter 3 has shown, many contact lens materials have hydrophobic domains at the surface. The function of surfactants relies on hydrophobicity; the hydrophobic components of the surfactant molecules will be attracted to the hydrophobic domains of the surface. The methods to assess this adsorption are discussed in this chapter. The air/water interface can be likened to the contact lens/water interface (the hydrophobic domains previously mentioned) and is used as a surrogate surface in these experiments. The adsorption behaviour at both of these interfaces will be similar.

Static and dynamic surface tension techniques and the assessment of critical micelle concentration (and its relevance to large surfactant molecules) are used to investigate a range of surfactants and surfactant-containing contact lens MPS. In order to investigate the role of surfactants in MPS, the surfactant needs to be examined separately. This removes the influence from any additional ingredients in the MPS. The data for a selection of commercially available MPS are presented here. In addition, the data for large non-ionic surfactants that are commonly used in surfactant-containing MPS is also presented.

The Food and Drug Administration (FDA) requires any contact lens care solution to have a surfactant concentration of at least its CMC. For simple surfactants this is the concentration when micelles start to form. Surface tension techniques are commonly used in accord with the ISO standard to measure the CMC. However, CMC determination in block copolymer systems is difficult, partly because these copolymers are frequently heterogeneous with respect to both composition and molecular weight. These high molecular weight surfactants can also form micelles with only a few molecules.

The data presented here will show the effect of surfactant concentration, molecular weight, molecular structure and hydrophilicity on surface tension and CMC.

4.1. Static Surface Tension

The static surface tension results shown here were acquired using the platinum Du Noüy ring method described in section 2.7.1. Static surface tension gives an indication of how many molecules are present at the surface.

Table 4.1.1 shows the static surface tension, the active surfactant contained in each MPS selected, and the surfactant molecular weight.

Table 4.1.1 Surfactant information of various commercially available contact lens MPS

Solution	Complete RevitaLens	Complete Easy Rub	All In One Light	Opti-free Express	Opti-Free RepleniSH	Synergi	Biotrue	ReNu Multitplus
Static Surface tension	39.9 ± 2	44.9 ± v2.2	48.8 ± 2.4	39.6 ± 2	37.7 ± 1.8	37.7 ± 1.9	43 ± 2.1	47.3 ± 2.3
Surfactant	Tetronic® 904	poloxamer 237	Poloxamer 188	Tetronic® 1304	Tetronic® 1304	Pluronic® 127	Tetronic® 1107	Tetronic® 1107
Molecular Weight	6700	7700	8400	10000	10000	12600	15000	15000

Figure 4.1.1 shows the static surface tension values, measured using the Du Noüy technique. The solutions have been arranged in surfactant molecular weight order. The data in table and the graph shows some variation (between 38-49 mN/m) between solutions without great discrimination.

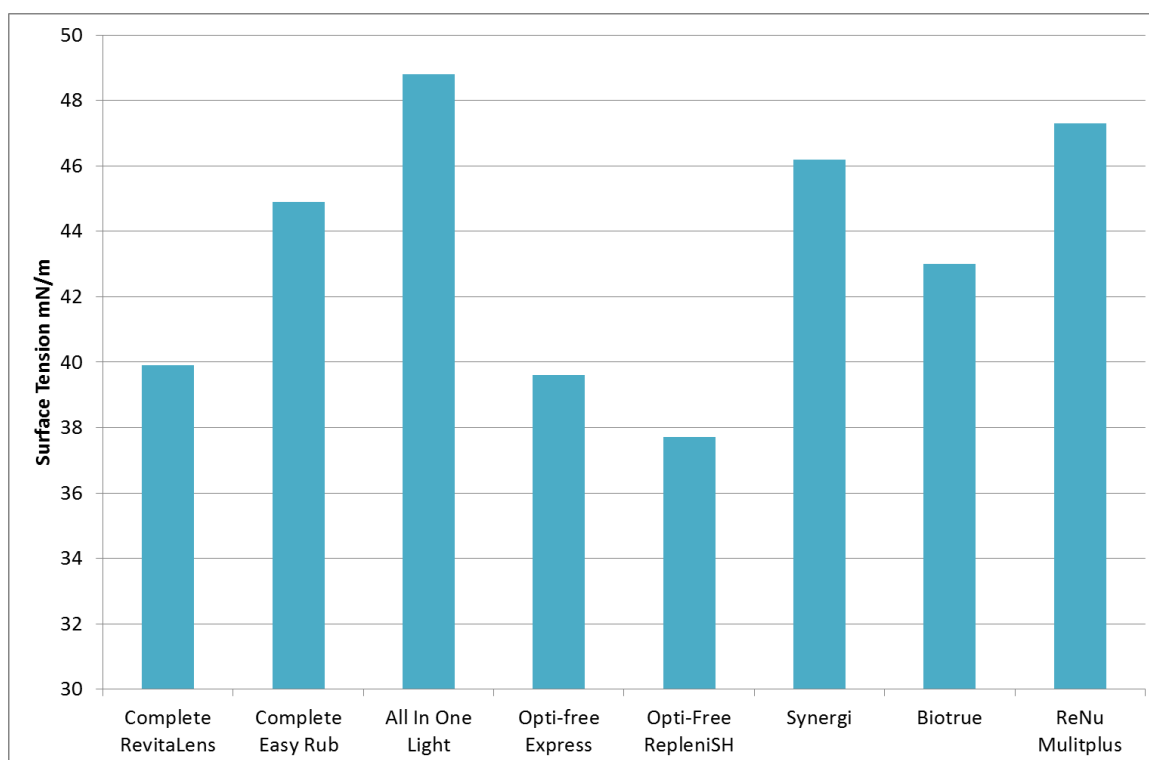


Figure 4.1.1 Static surface tension of various multi-purpose contact lens cleaning solutions (in ascending order of surfactant molecular weight)

The surfactant concentration is different in each MPS. This can be a cause for surface tension differences, especially if the surfactant concentration is around the CMC value. In these examples the static surface tension appears not to be dependent on surfactant molecular weight. The surfactant concentrations are often undisclosed and may be different for all the solutions, plus many contain more than one surface active ingredient.

Further on in the chapter (Figure 4.4.4), the cleaning efficiency of the MPS is investigated. There is a general link between the static surface tension and cleaning efficiency. The static values may be a more useful prediction of cleaning than the current FDA requirement of MPS having at surfactant concentration at or above the CMC [140].

The static surface tension values for all the MPS are all fairly similar. There is no simple correlation between the surface tension of the MPS and the surfactant concentration and other components contained in the MPS must also contribute.

Figure 4.4.5 (further on in this chapter) shows how the static surface tension can indicate how effective a contact lens MPS will clean. In general, the lower surface tension values, the more effective the solution is at cleaning.

Figure 4.1.2 shows the static surface tension of several surfactant solutions. Two concentrations were measured (0.1% and 1%) for these data. The measurements were taken in triplicate. The results are purely to provide an indication of the relative behaviour.

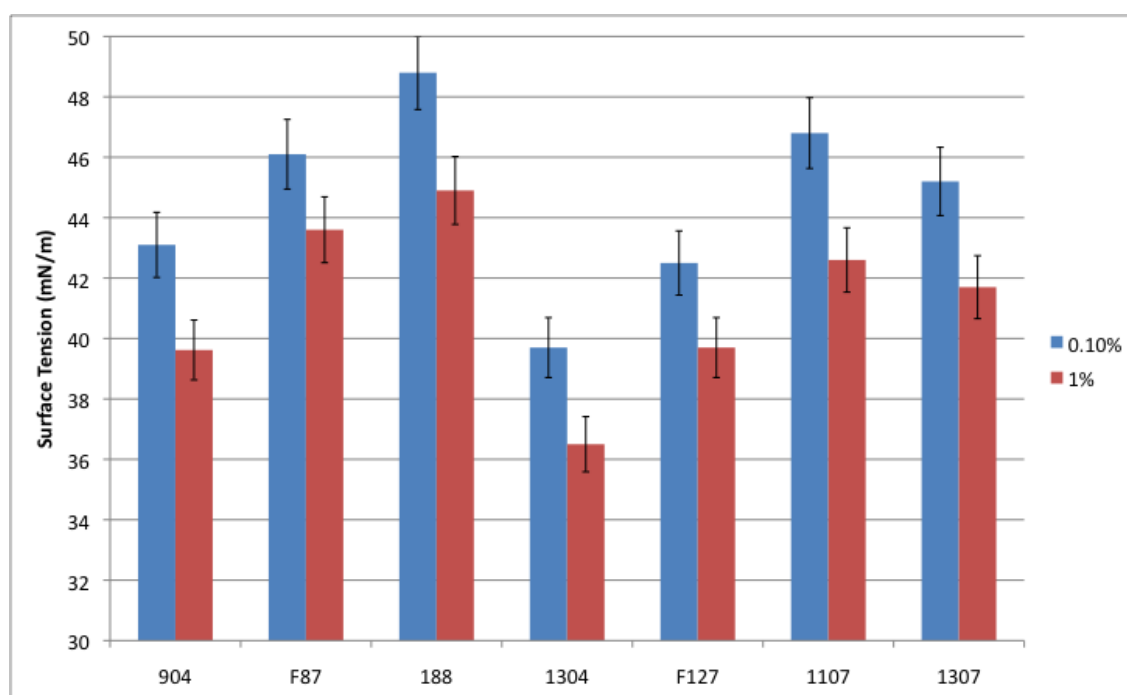


Figure 4.1.2 Static surface tension of several surfactant solutions at 1% and 0.1% concentrations

An increase in the surface tension value is observed as the surfactant concentration is reduced. This is to be expected, as there are fewer molecules at the surface. The behaviour of these surfactants however is sometimes too complicated to create or follow rules and surfactant concentration and surface tension is not a linear relationship. In addition to this, the molecular weight stated by the manufacturer is an average value. There will be a range of molecular weights contained within each surfactant solution. This heterogeneity in molecular weight will affect the surface tension behaviour as all molecules contribute to the static value.

The MPS could also contain other surface active ingredients that may attribute to the static surface tension. Total surfactant molecular weight is not the only factor contributing to surface tension. The structure and hydrophobicity of the molecule must also play a part. Pluronics® have two hydrophilic 'arms' and Tetronics® have four, this means the molecules aggregate differently and micelle behaviour will be different for each. It has been shown in the literature, that it is the molecular weight of the hydrophobic centre of these molecules, which dictates their behaviour. This chapter this point will be investigated further on in this chapter.

Static surface tension data alone is not sufficient; the dynamic surface tension gives quantitative measurements of another aspect. Dynamic behaviour is of particular interest in regards to cleaning. The molecular weight heterogeneity within the surfactants will also become apparent when the dynamic plots are analysed.

4.2. Dynamic Surface Tension

Dynamic surface tension principles have been previously explained in section 1.2.2. The dynamic method used here is the maximum bubble pressure technique. Two glass capillary probes of different diameters pass nitrogen gas through the sample of surfactant or MPS. The pressure difference between the probes allows for the surface tension to be measured. The gas flow rate can be varied and this in turn varies the surface agitation of the sample. The maximum bubble pressure method repeatedly agitates the surface of a solution. This disrupts the surfactant molecules that are arranged at the surface.

Pluronic® and Tetronic® molecules are larger than simple surfactants and they have more complicated structures. These large molecules take time to rearrange themselves, whereas simple low molecular weight molecules reach equilibrium much quicker. This is especially noticeable when the bubble frequency (agitation) is increased. The dynamic surface tension behaviour of a surfactant allows for predictions to be made on the size and hydrophobicity of the molecule. The data presented in this section are from dynamic surface tension measurements taken from the maximum bubble pressure method described in section 2.7.3.

The SensaDyne QC 3000 (SensaDyne Instrument Division, Arizona, USA) was calibrated at a low bubble speed, prior to each experiment. All experiments start at a low bubble speed and the speed was increased incrementally. As the gas flow rate is altered the calibration changes. This means that over the course of an experiment the measured surface tension value will be higher than the actual surface tension value (see Figure 4.2.1). It is possible to correct the surface tension data; however the focus of this chapter is to compare the surfactants and not absolute surface tension values.

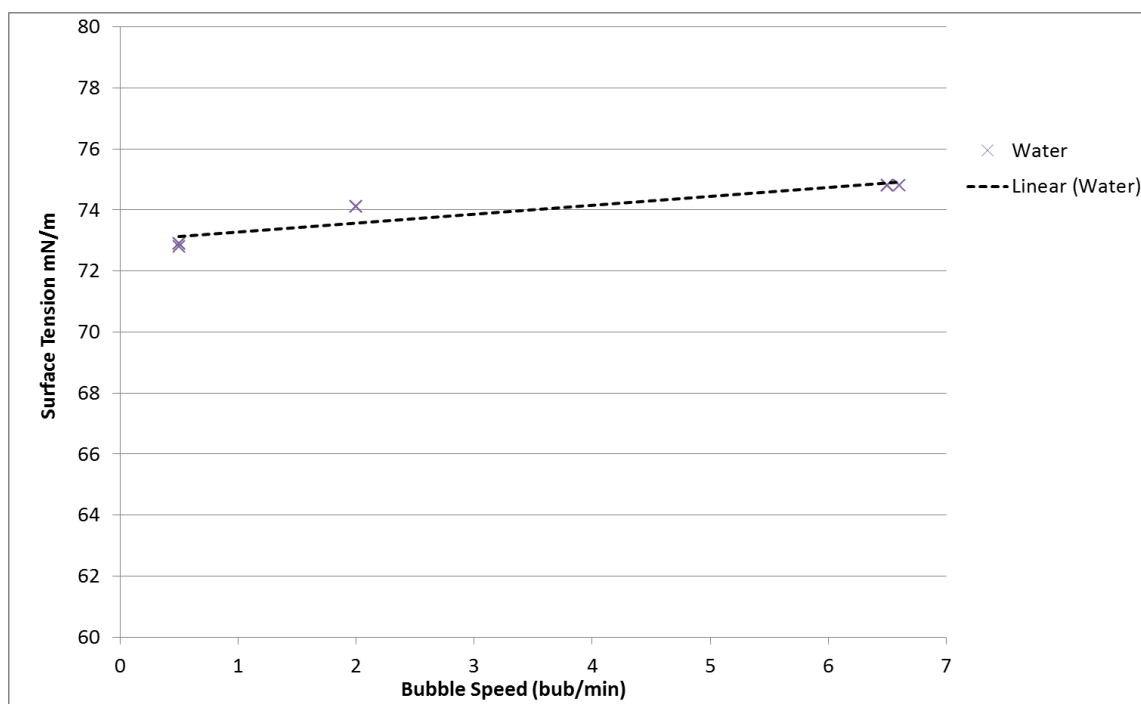


Figure 4.2.1 Dynamic surface tension measurements of HPLC water

4.2.1. Dynamic Surface Tension: Surfactants

Data values collected from the dynamic method are different from the static surface tension data values. Surface tensions are higher and surfactant differences are amplified under dynamic conditions. Figure 4.2.1.1 illustrates the surface tension differences between the two Tetronic® surfactants (1304 and 1307) that have the same hydrophobic molecular weight. Their hydrophile percentages differ by 30% (40%-70%). There are clear differences in both graphs, between the two surfactants. The static surface tension values differ by approximately 5mN/m (for both 1% and 0.1% concentrations). Whereas there is approximately 10mN/m between the dynamic surface tension values at 0.5 bub/min and over 20mN/m difference between the

surface tension values at 7bubs/min. Increased agitation decreases the ability of a surfactant to reduce surface tension.

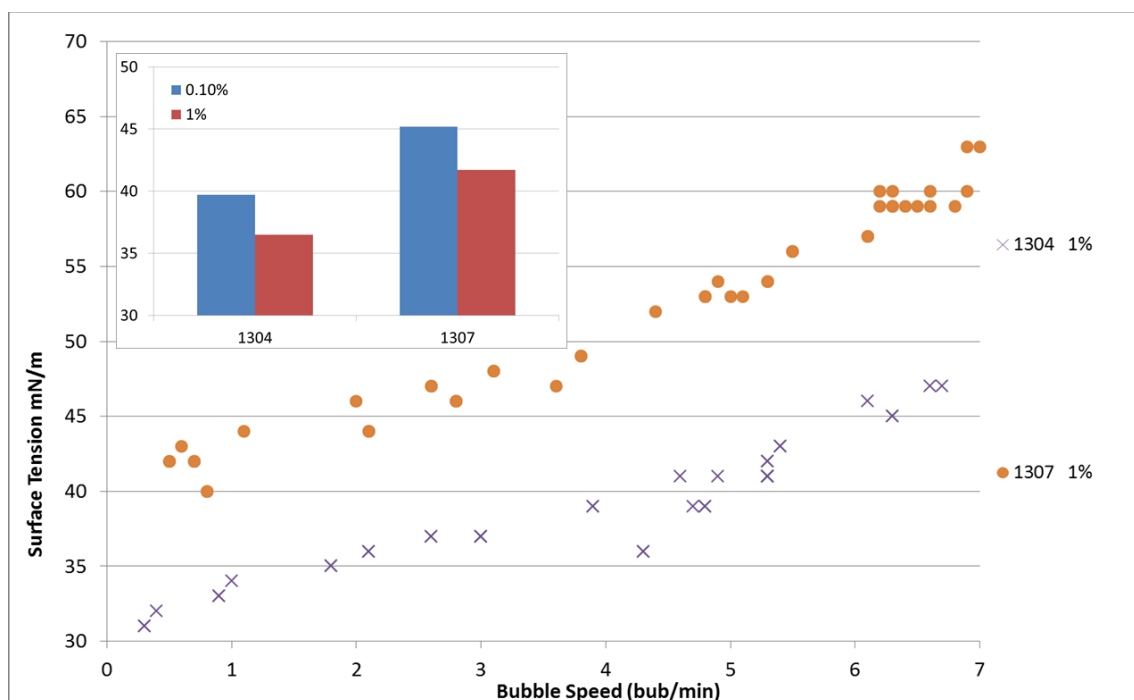


Figure 4.2.1.1 Static (inset) and dynamic surface tension data of Tetronics® 1304 and 1307

The 1304 molecules organise themselves more readily at the interface and reach equilibrium more rapidly in comparison to 1307. This is because of the difference in molecule hydrophobic proportion. A molecule of 1307 has a larger molecular weight than 1304 and 1307 is predominately hydrophilic, where 1304 is predominately hydrophobic. The effects of molecular weight and hydrophilicity on surface tension are explained in more detail throughout the chapter.

The dynamic surface tension data comprises of many data points and these plots can become confusing, so surfactants have been split into separate groups and graphs.

Figure 4.2.1.2 shows the different dynamic surface tension plots for 1% and 0.1% solutions.

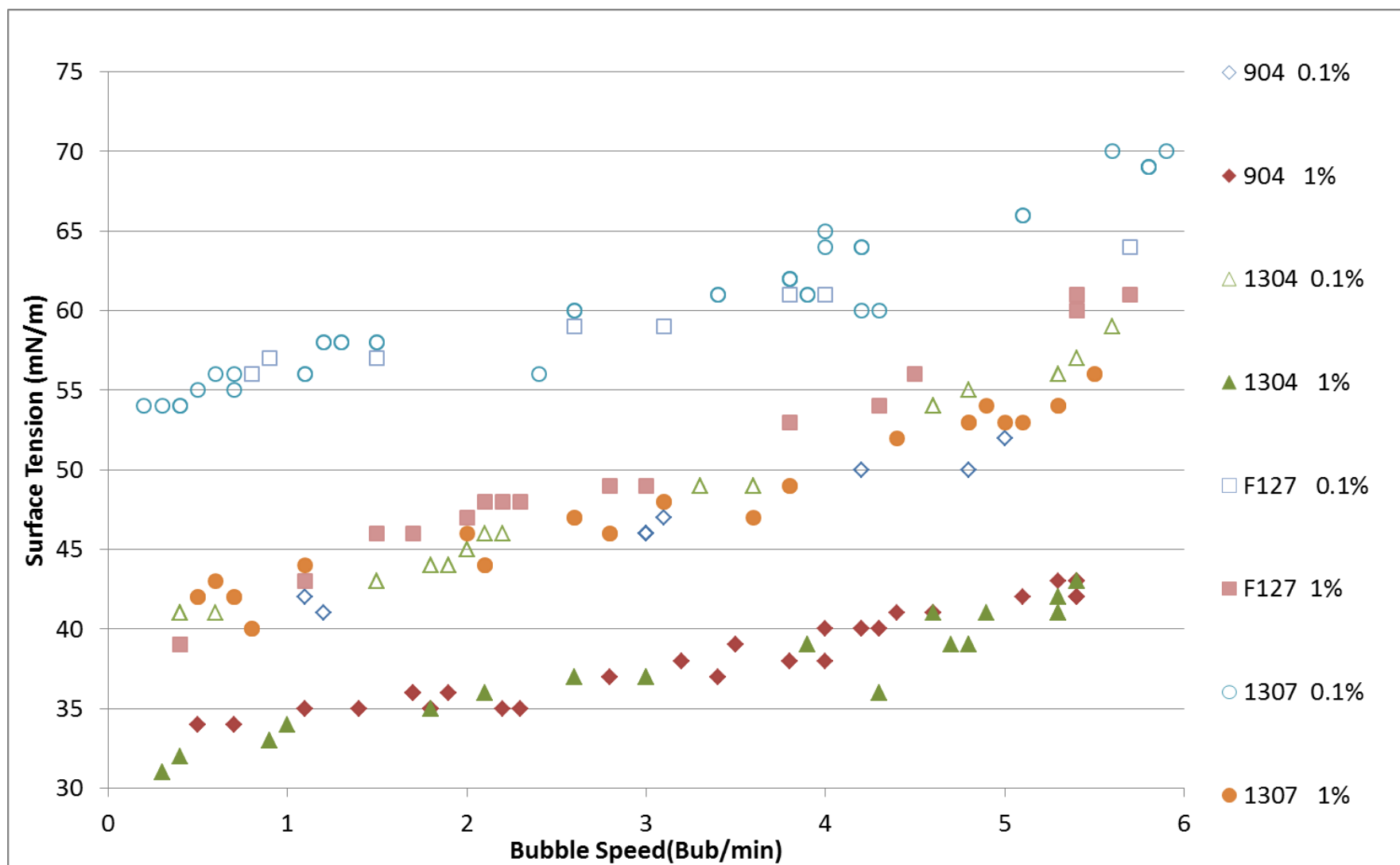


Figure 4.2.1.2
Dynamic surface
tension
behaviour of 1%
and 0.1%
Tetronic® and
Pluronic®
solutions

There are clear surface tension distinctions between hydrophobic and hydrophilic surfactants and differences between surfactant concentrations. In the centre of the graph are clustered data points, these are the plots for 0.1% hydrophobic surfactants and 1% hydrophilic surfactants. The hydrophobic Tetronics® 904 and 1304 have lower surface tension results than the hydrophilic surfactants (F127, 1107, 1037). The hydrophobic molecules aim to reach the surface as quickly as possible because of their water-hating nature. The predominantly hydrophilic molecules do not have as much hydrophobic drive to get to the surface and take longer to reach equilibrium.

The high concentration hydrophobic surfactant (904, 1304) solutions show the lowest surface tension values and the highest surface tension values are from the low concentration hydrophilic surfactant solutions (F127, 1307). The intermediate are a collection of data points, a mixture of high concentration hydrophilic (70%) and low concentration hydrophobic (40%). Here again in this graph we see the importance of the hydrophobicity, molecular weight and the concentration.

Figure 4.2.1.3 shows the dynamic surface tension behaviour of several hydrophilic Pluronics and Tetronics at 1% concentration.

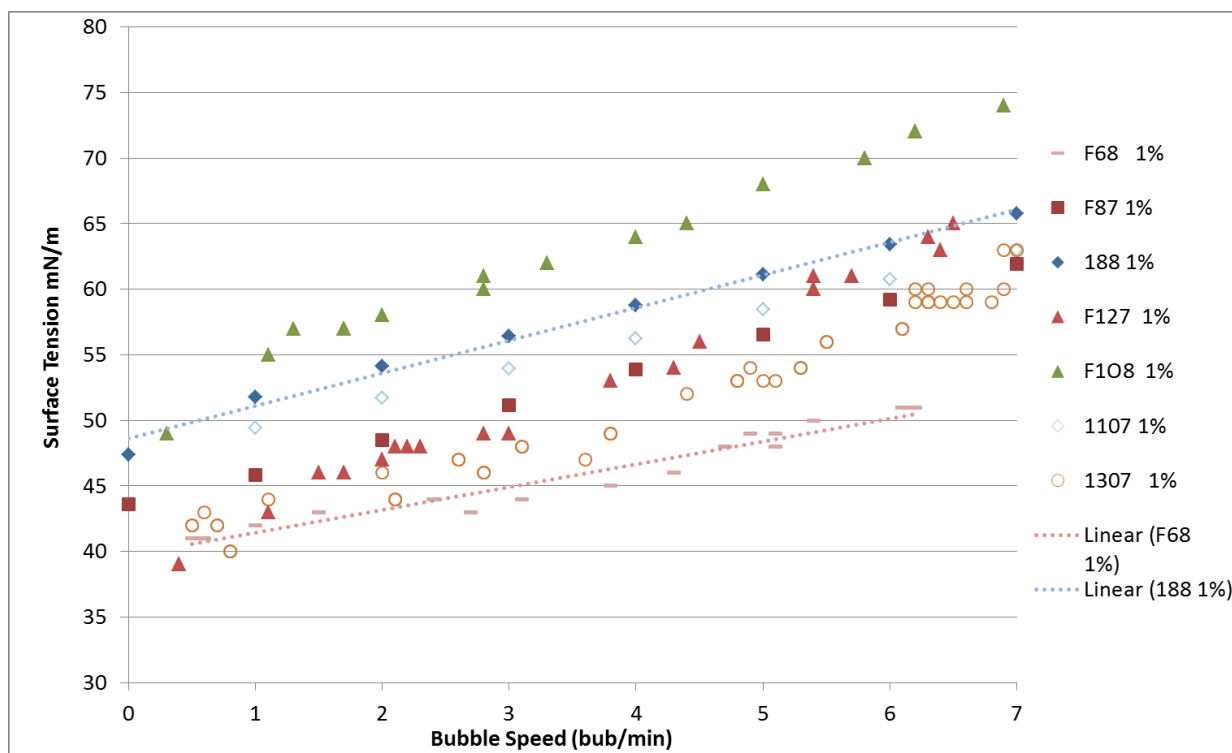


Figure 4.2.1.3 Dynamic surface tension of several hydrophilic triblock copolymer surfactants at 1% concentration at varying bubble speeds.

All of the surfactants presented in this graph are 70% or 80% hydrophilic (as denoted by the last number). The molecules all have different molecular weights and different surface tension plots.

There is a weak trend between molecular weight and surface tension. This follows the observations that were made from the static surface tension data. The higher molecular weight surfactants show higher surface tension values. As previously observed, molecular weight is not the only factor affecting the dynamic surface tension. It is important to reiterate that these surfactants are heterogeneous and in regards to molecular weight an average value is stated.

An interesting observation from this graph refers to the data presented for poloxamer 188. There are data plots for two poloxamer 188 surfactants, F68 is supplied by BASF® and 188 is from an unknown supplier. There are clear differences between the data plots (see dotted lines on Figure 4.2.1.3). This indicates considerable molecular differences. This anomaly is further investigated in section 4.3 where the critical micelle concentration of the both poloxamer 188s is measured.

Pluronic® F68 is not a widely used surfactant and the heterogeneity of its molecular weight and composition could well contribute to these surface tension effects. It may also be more hydrophobic than expected.

Figure 4.2.1.4 shows the dynamic surface tension of several hydrophobic surfactant solutions. The surfactants shown here are all 50% or 60% hydrophobic.

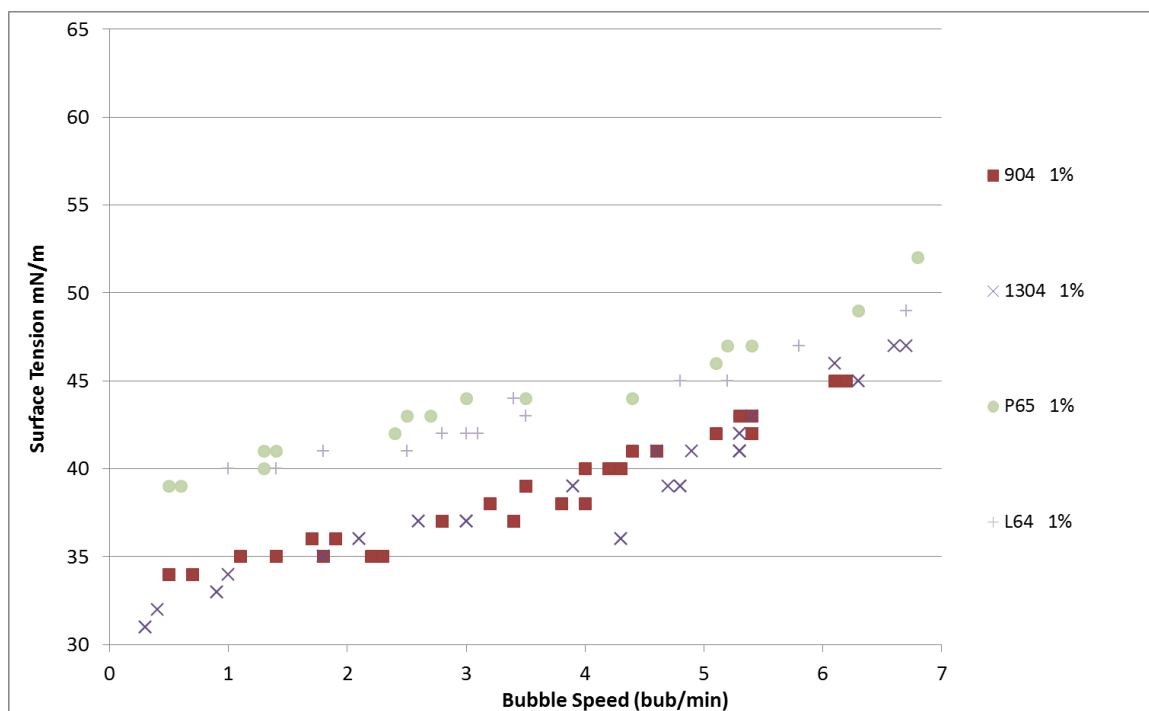


Figure 4.2.1.4 Dynamic surface tension of several hydrophobic triblock copolymer surfactants at 1% concentration.

Pluronic® P65 and L64 behave similarly to each other in this graph. There is very little difference between the molecular weights of these two surfactants and it is unsurprising that the dynamic surface tension measurements are so similar. It is observed from this graph that the plot gradients for the larger molecules are steeper than the plots for the smaller molecules. This point compliments conclusions and data found in Holland et al[141] and Booth et al[142]. Both papers show that molecular weight, especially the hydrophobe block, affects the CMC of a surfactant. The larger molecules have lower critical micelle concentrations (see Figure 4.2.1.6).

This graph shows a difference between molecular weights, the higher molecular weight surfactant solutions (904 and 1304) have a lower surface tension for all bubble speeds. It is however a contrast to the diversity shown in the hydrophilic surfactant

plots in Figure 4.2.1.3. The molecular weight of the hydrophobic surfactant differs by a factor of three and the surface tension plots are almost parallel to each other. The molecular weights of the hydrophilic surfactants shown only differ by a factor of 2 and there is a diverse range of surface tension plots. From this data it seems that hydrophobic drive is the biggest influence in the prediction of dynamic surface tension behaviour. The more hydrophobic the surfactant, the greater the hydrophobic drive to get to the surface; these surfactants reach equilibrium more readily.

Hydrophobic drive is clearly important and it is possible to see that with these high molecular weight block copolymer surfactants, as the surface is disturbed so the surface tension rises. The more readily the surface tension comes to equilibrium the lower the surface tension will be.

It is difficult to see some trends due to heterogeneous molecular weights. There are complex interactions between the hydrophobic drive, the ability of the molecular weight and the complexity of the structure are all involved with organisation at the surface.

Figure 4.2.1.5 presents dynamic surface tension data for all of the surfactants on the same graph.

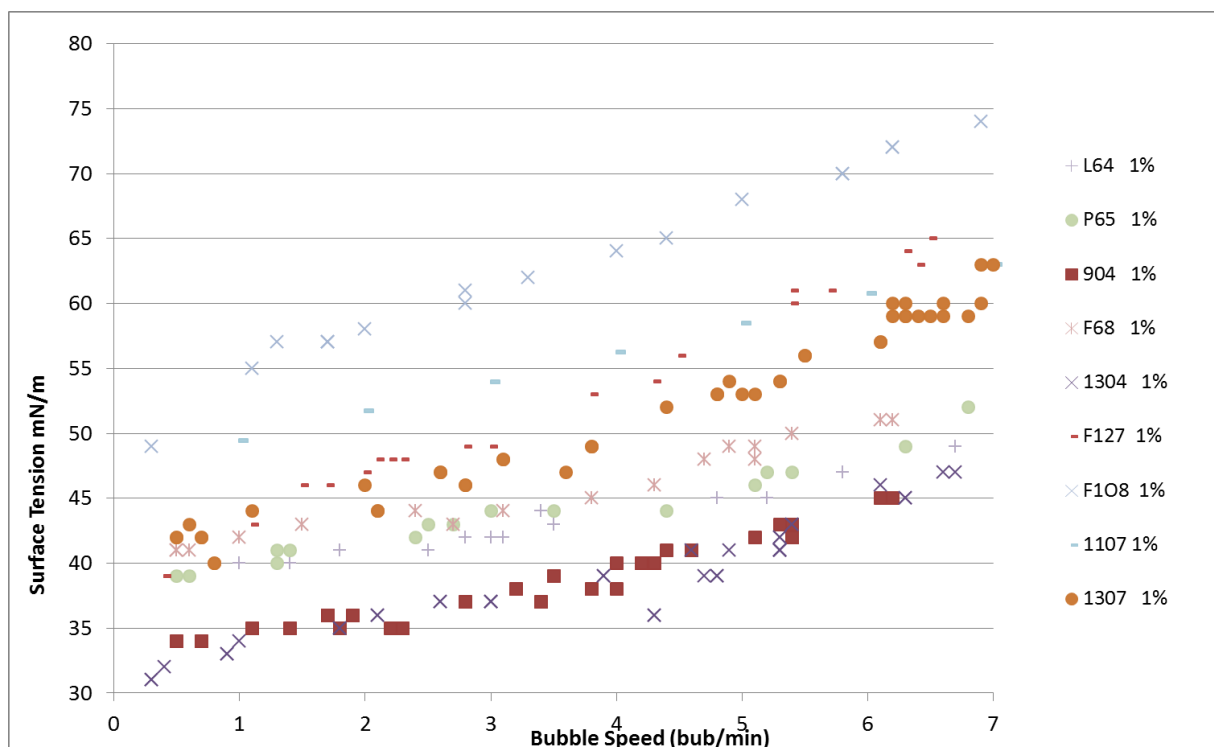


Figure 4.2.1.5 Dynamic surface tension of 1% Tetronic® and Pluronic® solutions at varying bubble speeds

The poloxamers have different surface tension values and different slope gradients. However, when the graph is so congested, plot gradients for each surfactant are difficult to visualise in this way. The individual plot gradients are used further on in the chapter and these differences are investigated. The plot gradient shows more value in relation to molecular weight.

Figure 4.2.1.6 shows CMC literature values against their total molecular weight and the molecular weight of the hydrophobic polypropylene block.

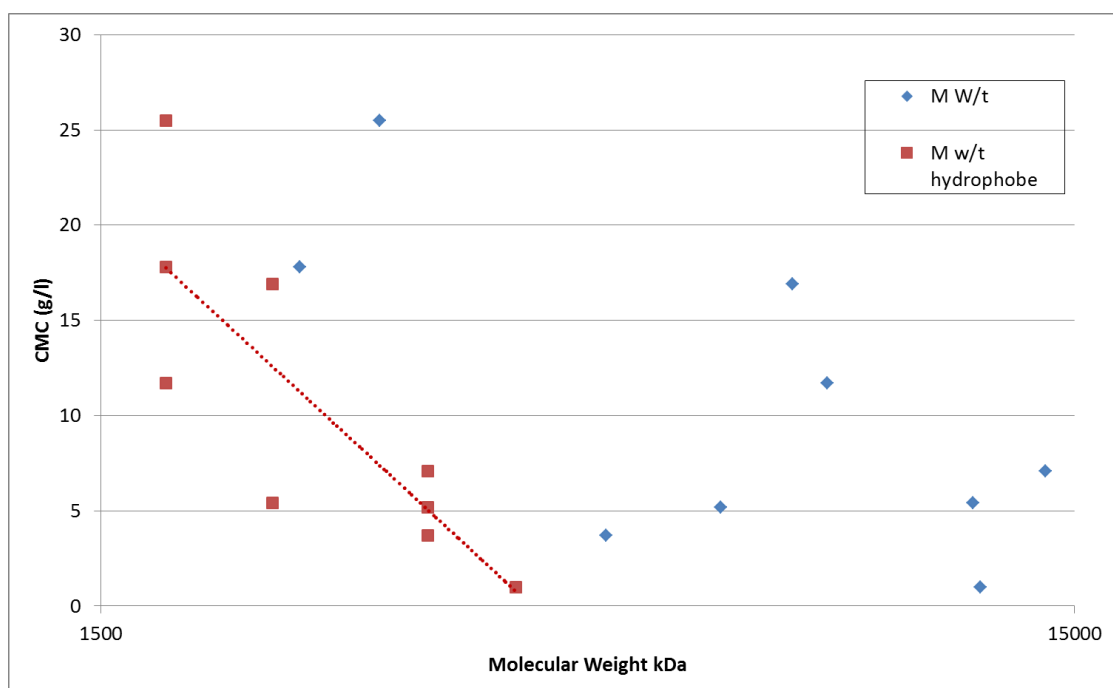


Figure 4.2.1.6 Collected CMC values for Pluronic® surfactants and their total molecular weight and the molecular weight of their hydrophobic block.[141, 143]

It has been previously mentioned that the hydrophobic block of Pluronics® and Tetronics® has the most influence in their behaviour under dynamic conditions. Figure 4.2.1.6 shows there is less data point deviation when the hydrophobic molecular weight is used as an alternative for total molecular weight. Statical analysis confirmed that there was a greater correlation between the CMC and the molecular weight of the hydrophobe (-0.82) compared with the correlation between the CMC and the total molecular weight (-0.63). The correlation between CMC and hydrophobic molecular weight was significant at the 1% level. For this reason Figure 4.2.1.7 presents data in comparison to surfactant hydrophobe molecular weight.

Figure 4.2.1.7 shows the dynamic surface tension gradients against the molecular weight of the hydrophobic block.

A linear trend line was added for each surfactant and the line gradient noted. From work presented in the literature, the high molecular weight surfactants are expected to have higher gradients[142]. Although there is some broad comparability in the previous figures, this graph is much more effective.

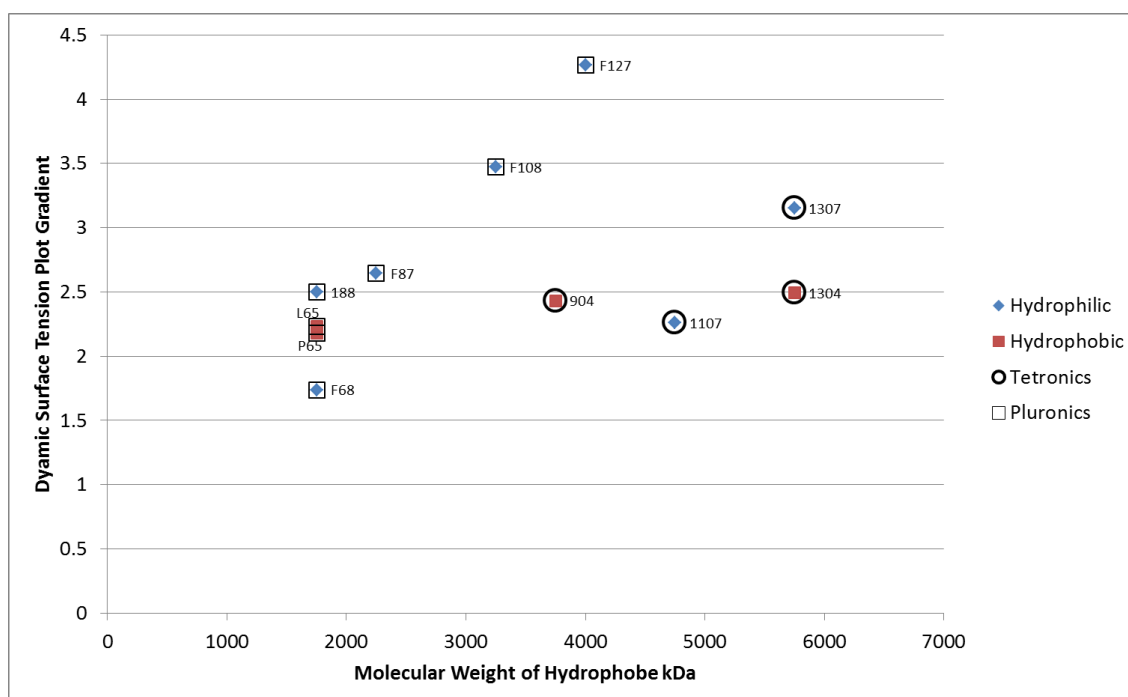


Figure 4.2.1.7 Surfactant molecular weight against plot gradients from Figure 4.2.1.3 and Figure 4.2.1.4

There is a clear correlation for all the surfactants presented. As the molecular weight of the surfactant increases so does the gradient. There is a more marked difference with the hydrophilic surfactants than the hydrophobic. There are also observed differences between Pluronics® and Tetronics®. This implies that there are additional factors that affect the dynamic surface tension behaviour, including molecular structure.

There is a less noted difference between the hydrophobic surfactants. Their graph plots are nearly parallel to each other in Figure 4.2.1.4. This could be because the molecular weights for the hydrophobic surfactants shown here are lower than the molecular weights for the hydrophilic surfactants. The conclusions from Booth et al [142] suggest that it is the size of the hydrophobic block that dictates the dynamic surface tension behaviour, this point is also made elsewhere in the literature[144].

Statistical analysis of the data found that the correlation between the hydrophobic molecular weight of the Pluronics® and the Dynamic surface tension plot gradient was highly significant (0.96) at the 1% level. This was not the case for the Tetronics®, the correlation was not statistically significant (0.6).

There is more to be learned from the surface tension of hydrophobic and hydrophilic surfactants, but the simple points are as follows:

- For initial static surface tension experiments, the molecular weight shows little effect on the measured values. It is the surfactant concentration that has the greatest effect.
- It is important to understand the relevance of the dynamic behaviour in regards to cleaning. The dynamic surface tension is very much part of the antibacterial activity (bacteria is removed from the surface). With this knowledge it is important to revisit the Multi-purpose solutions and observe how they behave under dynamic conditions.
- It can be seen on both hydrophobic and hydrophilic graphs that the surfactant plots fan out as the bubble speed increases. This is even more noticeable for the hydrophilic molecules.
- Direct comparison is possible for surfactants such as 1304 and 1307. For many of the other surfactants there are too many unknowns to make a complete analysis and the complexity of the effects is considerable.
- Hydrophobic drive seems to be the greater influence above all other variables. This is demonstrated by hydrophobic and hydrophilic plot differences. When there is a high hydrophilic proportion in a molecule, molecular weight has a greater effect than when there is a high proportion of hydrophobe. High molecular weight hydrophilic surfactants do not have a great drive to get to the surface and can be hindered further by chain entanglement.

4.2.2. Dynamic Surface Tension: Multi-purpose solutions

The previous section has shown that dynamic surface tension measurements display greater differentiation between surfactants. The differences are particularly noticeable at high bubble speeds. Many contact lens MPSs contain different surfactants and at different concentrations. This can be because of surfactant properties or to address customer issues, such as symptomatic customers (Sauflon's 'All in One Light®' is produced for customers with sensitive eyes. 'All in One Light®' contains less surface active ingredients than 'Synergi®').

Figure 4.2.2.1 shows the dynamic surface tension plots for three Sauflon MPS solutions.

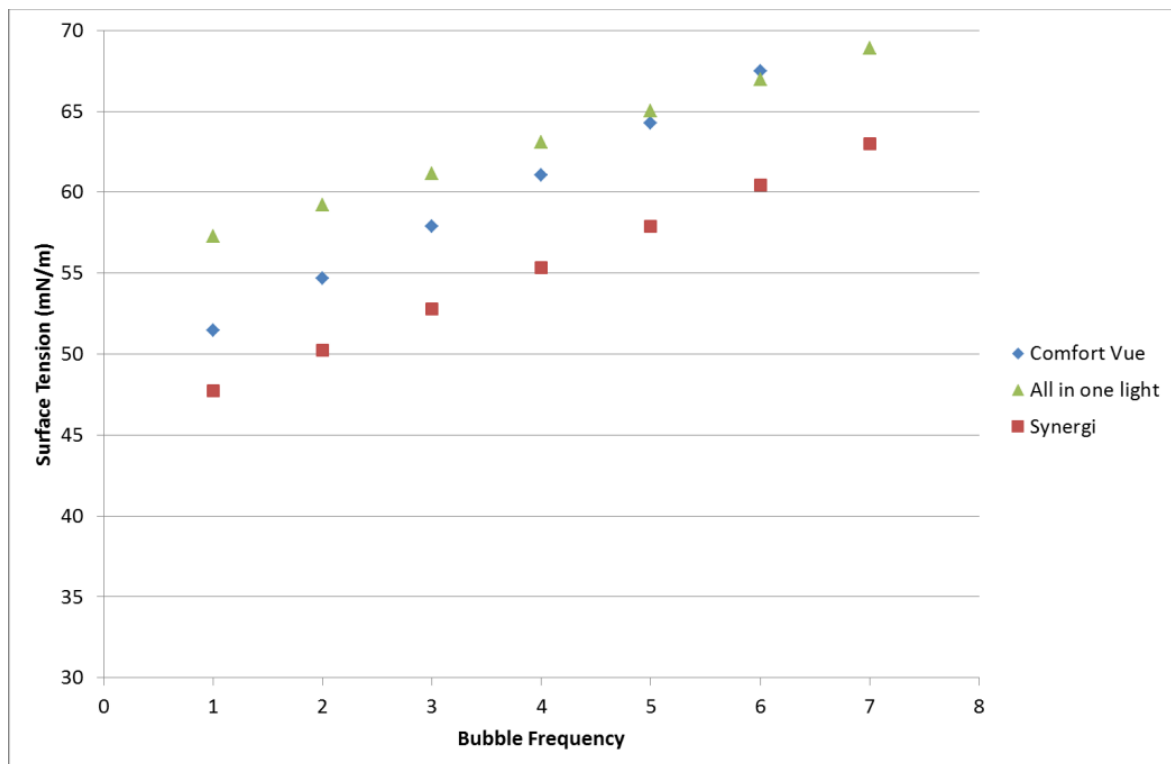


Figure 4.2.2.1 The dynamic surface tension for a selection of Sauflon multi-purpose contact lens cleaning solutions at varying bubble speeds

It is clear from this graph that each solution contains either a different surfactant and/or at a different concentration.

Figure 4.2.2.2 shows the same three MPS solutions in addition to the dynamic surface tension plots of several surfactants at various concentrations.

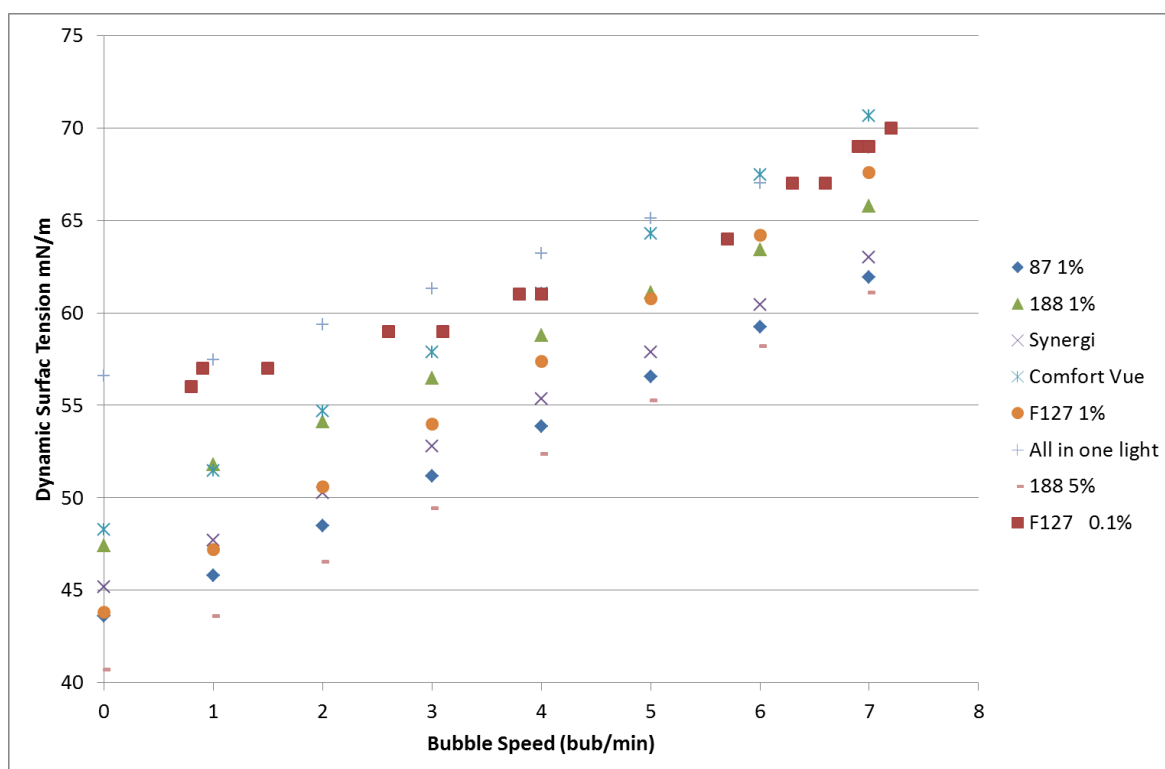


Figure 4.2.2.2 The dynamic surface tension for a selection of Sauflon multi-purpose contact lens cleaning solutions at varying bubble speeds with additional surfactant plots

There is usually more than one ingredient in a MPS and this could include an additional surface active component. Synergi® has initial surface tension values similar to F127 but the plot for Synergi® is not as sharp as F127. As the bubble speed increases the Synergi® plot tends towards the plot for Pluronic® 87. The data for Synergi® suggests there is a combination of at least two surfactants, and one of them has a relatively small molecular weight. The Comfort Vue plot runs parallel to the F127 plot, but starts at a higher surface tension.

Figure 4.2.2.3 shows the dynamic surface tension plots for several commercially available contact lens multi-purpose solutions.

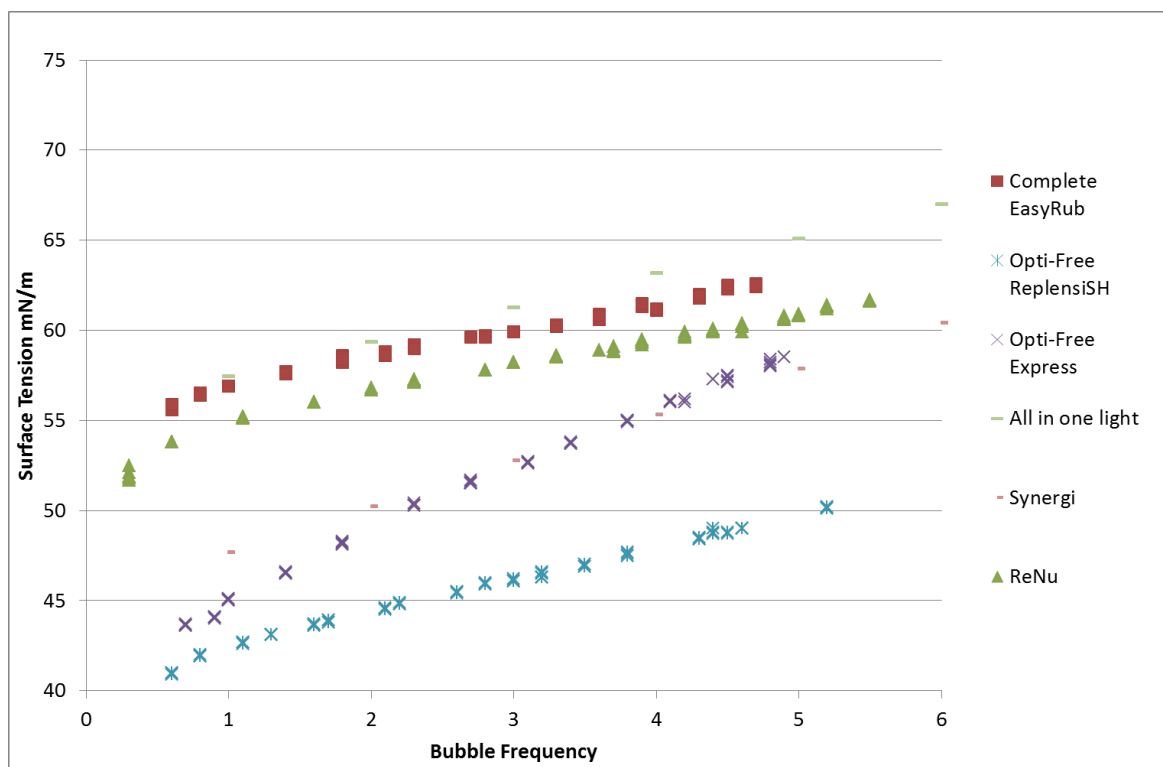


Figure 4.2.2.3 Dynamic surface tension of a selection of commercially available contact MPS solutions at varying bubble speeds

This graph clearly shows that there are different surface active ingredients in the MPSs. Most obviously is the difference between the Opti-Free® solutions. Both Opti-Free® RepleniSH and Express contain Tetronic® 1304 (that has an average molecular weight of 10000), RepleniSH has an added low molecular weight surfactant, ethylenediamine tri acetic acid, this has a molecular weight of 307g/mol. The dynamic behaviour is dominated by the lowest molecular weight surfactant present in the solution.

The dynamic surface tension behaviour of a surfactant can indicate differences in size and hydrophobicities. These differences are clearly shown in the separate surfactant plots in section 4.2. Contact lens MPS contain surfactants, and often a combination of other ingredients. The dynamic method allows for differences to be noted between solutions. However, it is difficult to predict the make-up of the solution as so many variables (surfactant concentration, molecular weight, hydrophobicity and a combination of ingredients) affect the surface tension behaviour.

4.3. Critical micelle behaviour of multi-purpose and surfactant solutions

As explained in Chapters 1 and 2 the critical micelle concentration (CMC) is the concentration at which surfactant molecules will start to aggregate and form micelle structures.

Figure 4.3.1 shows the physical properties of sodium lauryl sulphate (a simple surfactant) behaviour depending on surfactant concentration and highlights the area where the CMC would occur.

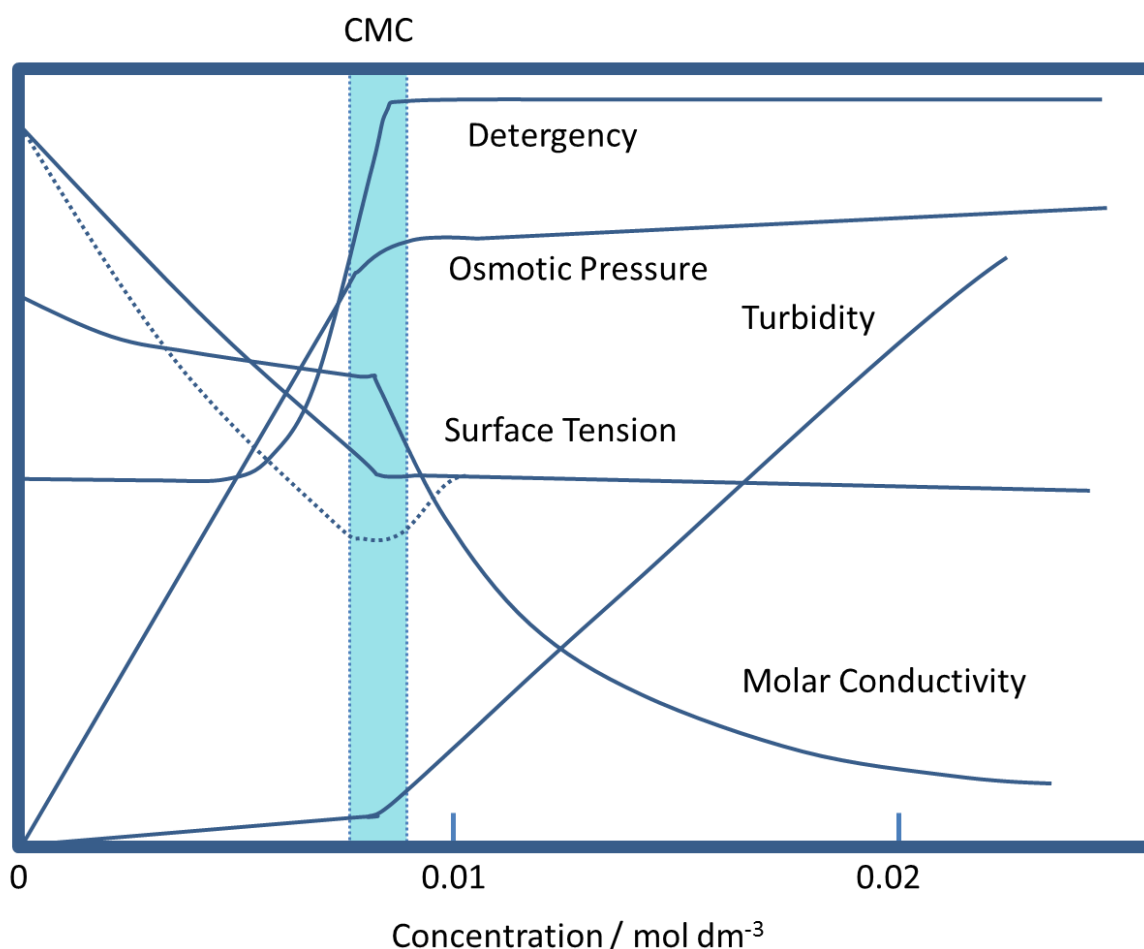


Figure 4.3.1 Physical property curves of a simple surfactant[7, 145]

The CMC is often used as a benchmark value for surfactant containing MPSs, where a surfactant solution is required to be at a concentration above the CMC to provide sufficient cleaning performance[140]. This graph is similar to that shown in Figure 1.2.4.1 with the addition of a detergency curve. Detergency is essentially the cleaning power of a surfactant. In regards to contact lens MPS, it is important that the solution cleans the lens sufficiently for reinsertion into the eye. The detergency of the

surfactant is at its highest in the CMC area, this is where the surface tension starts to plateau, and why surface tension measurements are often used to measure CMC. ISO standard 4311 describes a surface tension methodology in which to measure the CMC [146]. Intuitively from a cost point of view, it is very important for cleaning solution manufacturers to only use as much surfactant as is needed.

The critical micelle concentration behaviour of large polymeric surfactants is markedly different from the observed behaviour of simple surfactants. The difference is caused by the size and shape of the molecules. Section 1.13.1 explains how the critical micelles concentration increases as the molecular weight of the surfactant decreases. So it can be possible to predict the CMC if the molecular data for the surfactant is known. For simple surfactants, the CMC is an obvious inflection point where the surface tension ceases to reduce as shown in Figure 4.3.1. For more complicated surfactants such as Pluronics® and Tetronics® or solutions where a mixture of surfactants have been used, the CMC is shown as a curved transition. There is clearly still some difficulty in interpreting the behaviour of these materials that are heterogeneous with respect to both molecular weight (an average molecular weight is stated) and heterogeneous in relation to composition (a point that will become clear for poloxamer 188 and Pluronic® F68LF). In a simple surfactant a classical micelle is necessary to remove and transport the hydrophobic debris from the surface. With these high molecular weight polymeric triblock surfactants, heterogeneous in terms of both molecular weight and composition, each molecule can resemble a micelle formed of many smaller surfactants. So the concept is not the same for both types of surfactant, and CMC data do not resolve themselves into the sort of graphs that the classical low molecular weight surfactants show.

The data shown in Figure 4.3.2 shows the dynamic surface tension values of hydrophilic Pluronic® solutions over a range of concentrations.

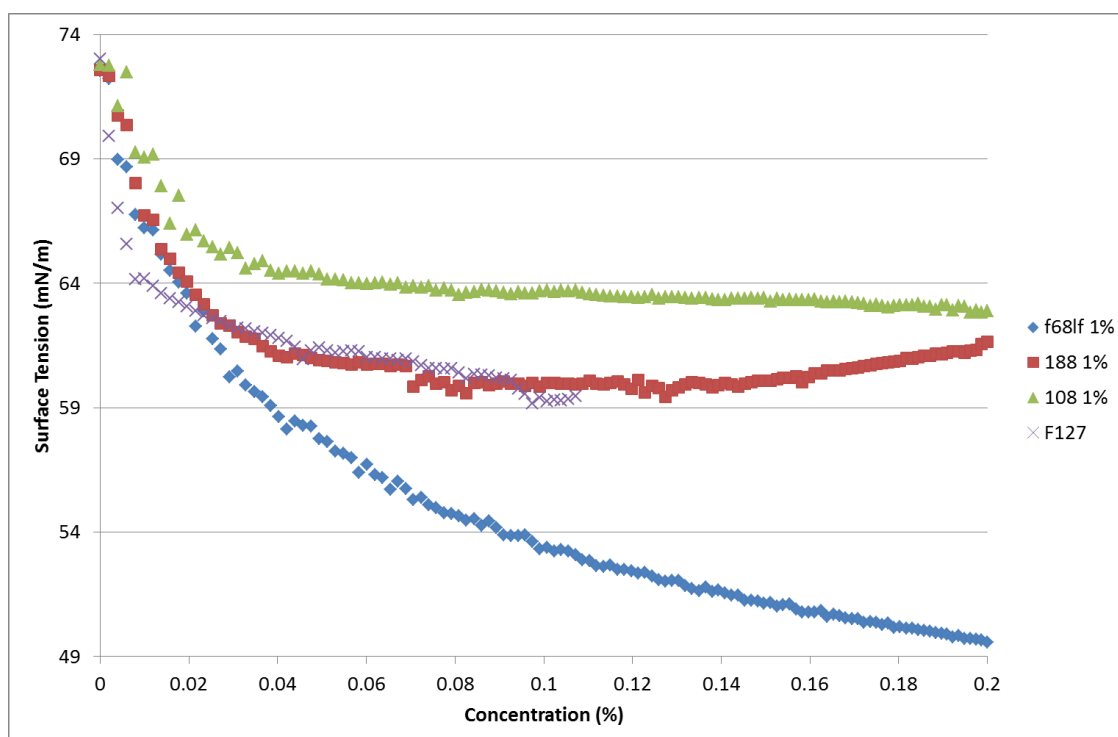


Figure 4.3.2 Dynamic surface tension of hydrophilic Pluronic® solutions over a range of concentrations

Initially this graph had Pluronic® F108, Pluronic F127 and poloxamer 188 (equivalent to Pluronic F68) data only. The molecular weights for these surfactants are 14600g/mol, 12600 g/mol and 8400 g/mol respectively; there should be an obvious difference between the CMC values. There is a clear difference between each surfactant. From visual analysis, the CMC inflection point (approximately) moves further to the left of the graph as the surfactant molecular weight increases. The CMC reduces as the molecular weight increases (see Figure 4.2.1.6).

The graph above shows that the data for F127 and 188 overlaps and behaves very similar. This was not the expected result because the molecular weights for these surfactants are quite different. The same experiment was performed using F68lf from a different commercial source to compare with the poloxamer 188 plot. The data for F68lf behaves as would be expected for its molecular weight. F68 and poloxamer 188 are thought to be the same surfactant, the surface tension data suggests otherwise. Poloxamer 188 could possibly contain a greater number of different chain length poloxamers but the average molecular weight would be the same as F68. The

molecular weight standard deviation of poloxamer 188 would then be much greater than that of F68.

The surface tension for poloxamer 188 starts to increase again as the concentration increases. This is a phenomenon observed in hydrophilic high molecular weight surfactants, such as F127, which become increasingly viscous at high concentrations. This is more marked in the hydrophilic surfactants with high molecular weights such as poloxamer 188 and F127 see Figure 1.13.1.1 in Chapter 1. When a Pluronic® or Tetronic® solution is more concentrated in solution, hydrophilic entanglement can occur.

Figure 4.3.3 shows the static CMC behaviour of hydrophilic surfactants. All surfactants shown have an inflection associated with critical aggregation behaviour.

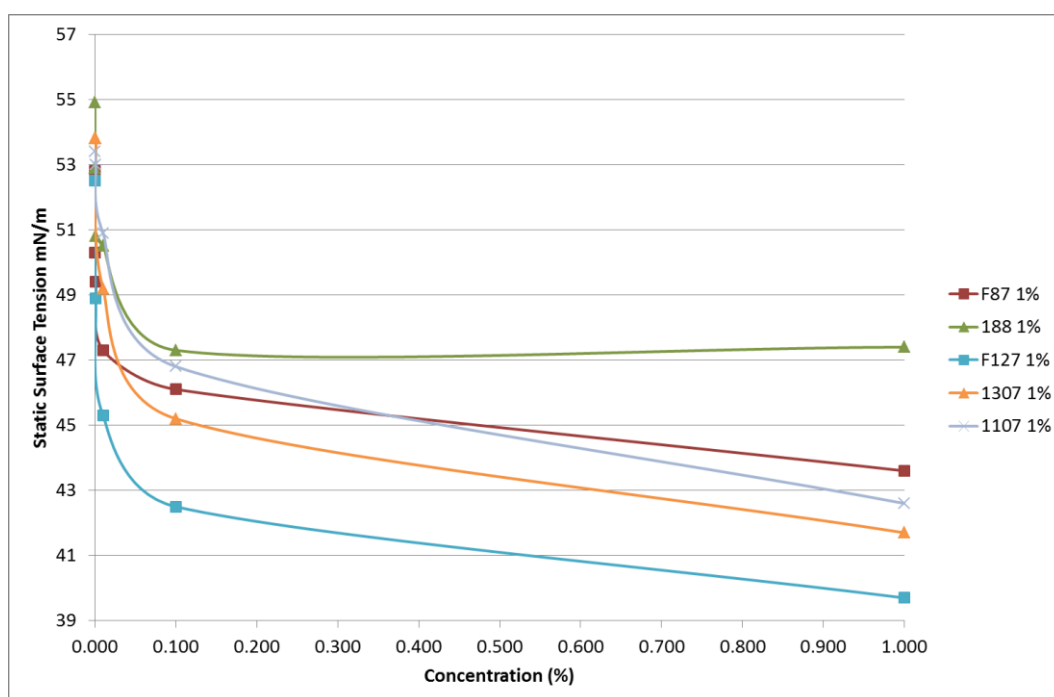


Figure 4.3.3 Static surface tension of hydrophilic Pluronic® and Tetronic® solutions over a range of concentrations

Figure 4.3.4 shows the change in static surface tension of a range of MPS at various dilutions expressed in terms of fractional concentration of the MPS.

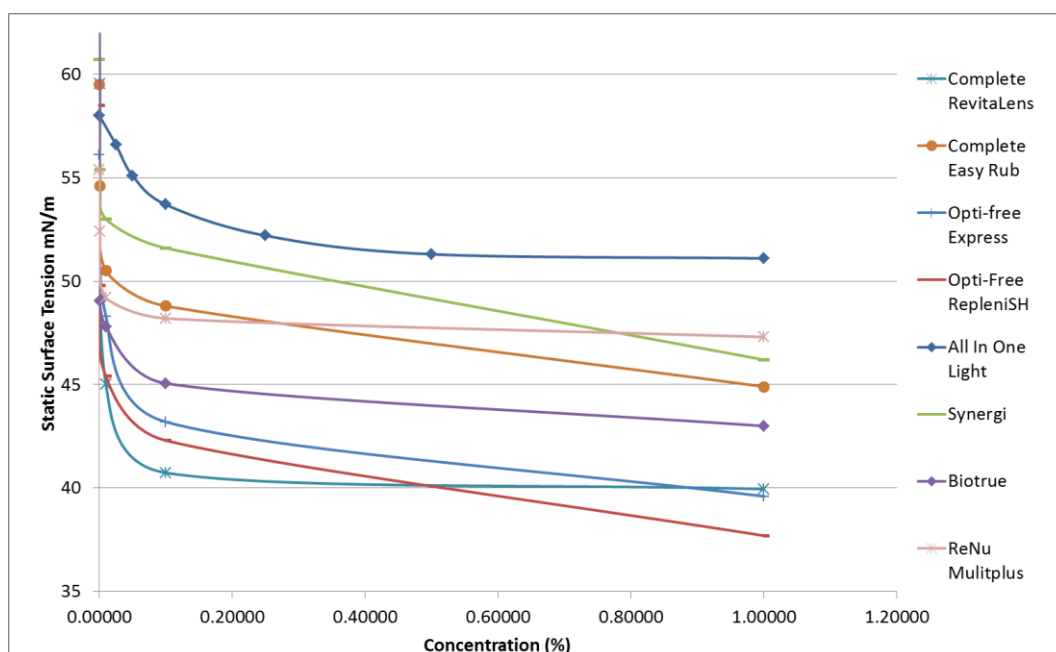


Figure 4.3.4 Static surface tension of several contact lens cleaning solutions over a range of concentrations

The surface tension for Opti-Free® express, RepleniSH, Synergi® and Complete® easy rub are still falling. This illustrates that the surfactant concentration in the multipurpose solution is above that of the critical micelle concentration.

The most effective MPS in terms of lipid removal is not characterised by a low and distinct CMC, even when many experimental points are collected using dynamic surface tension. So the CMC is not an indication of cleaning ability.

Figure 4.3.5 shows how ST and CMC can be affected by bubble speed and how the CMC is difficult to determine in larger triblock surfactants.

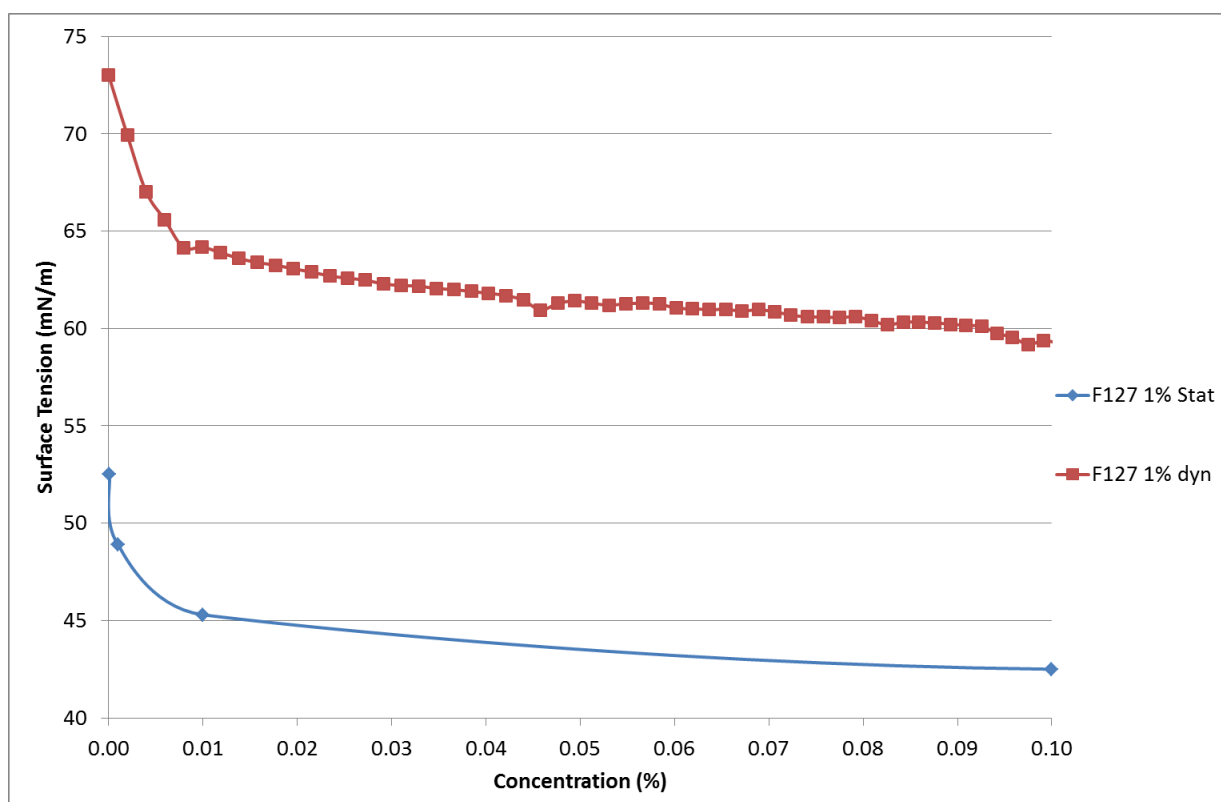


Figure 4.3.5 Static and Dynamic surface tension of Pluronic® F127 over a range of concentrations

For both sets of data there is a curved transition for the CMC, not an obvious inflection point. The static surface tensions measurements are almost 20mN/m lower than the dynamic measurements and the CMC transition appears earlier (lower CMC) for the static plot. This could be because of the reduced number of data points on the static plot.

The data presented in Figure 4.3.6 shows the values recorded by surface tension and refractive index measurements. The surfactant concentration was varied for the solutions analysed.

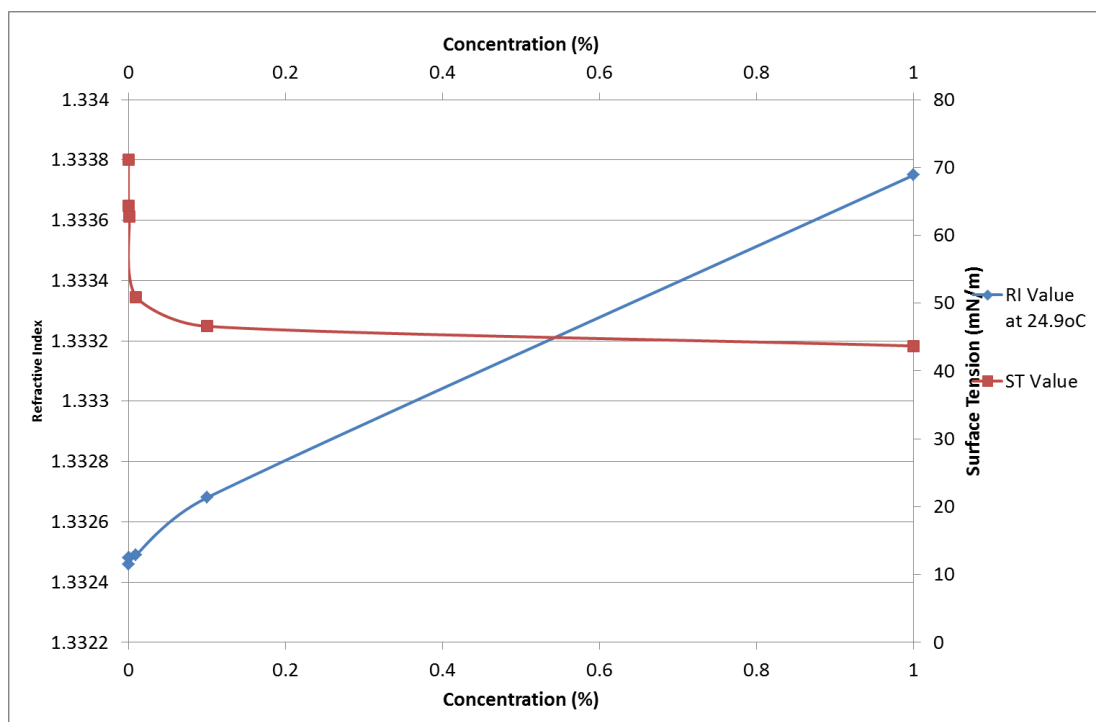


Figure 4.3.6 Refractive index and static surface tension measurements of Tetronic® 1307 over a range of concentrations

As previously mentioned, a small sample volume is important for the creation of an eye model, the refractive index methodology allows for volumes as small as 100µl to be analysed. The refractive index measurements do not vary much at low surfactant concentrations. The surface tension measurement changes are more obvious at low surfactant concentrations, and plateau after the CMC value. A larger sample of solution is needed to measure the surface tension (5-10ml for a regular sized Du Noüy ring). Although sample size is important when creating an eye model, For the work presented in this chapter and the chapters to follow, distinction between concentrations is essential in order to detect surfactant at low concentrations.

4.4. Discussion and Conclusion

This chapter presents surface tension data of several Pluronics®, Tetronics® together with contact lens multi-purpose solutions. MPS are used to complete a function that was previously completed by separate solutions. The ‘all in one’ solution needs to be able to clean a contact lens and it needs to be benign enough to be put straight into the ocular environment. For these reasons polymeric antibacterials and polymeric surfactants are used in current MPSs. These high-molecular weight molecules are less

able to penetrate the corneal cells and therefore cause less distress to the eye and tear film lipid layer.

Figure 4.4.1 shows that a surfactant has to do many things to successfully clean a surface.

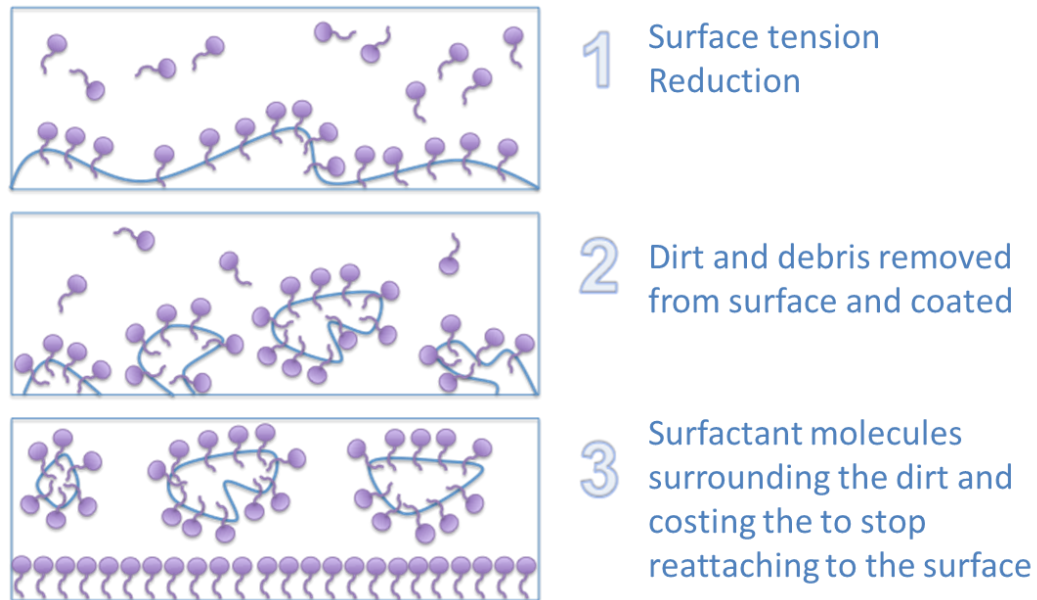


Figure 4.4.1 A diagram of how simple surfactant molecules can remove dirt and debris from the surface and coat the surface to reduce the dirt and debris reattaching.

The surfactant molecules attach to dirt and debris on a surface and by lower the surface tension of the liquid, surround and coat any dirt and in turn the interfacial tensions between oil (dirt and debris) and water[77] and condition the surface. It has been shown in the literature [41] that the wettability of contact lenses is increased by the surfactant molecules conditioning the surface. The surface modification is not permanent and the level to which a surfactant persists is the focus of Chapters 5 and 6.

The Pluronics® and Tetronics® vary in structure, molecular weight, hydrophilicity and concentration and it is clear that each property has an influence on how the surfactant behaves under certain conditions.

The size of a surfactant molecule influences its dynamic behaviour as does the shape and structure of the molecule. Figure 4.4.2 shows the approximate size and structure of three surfactants.

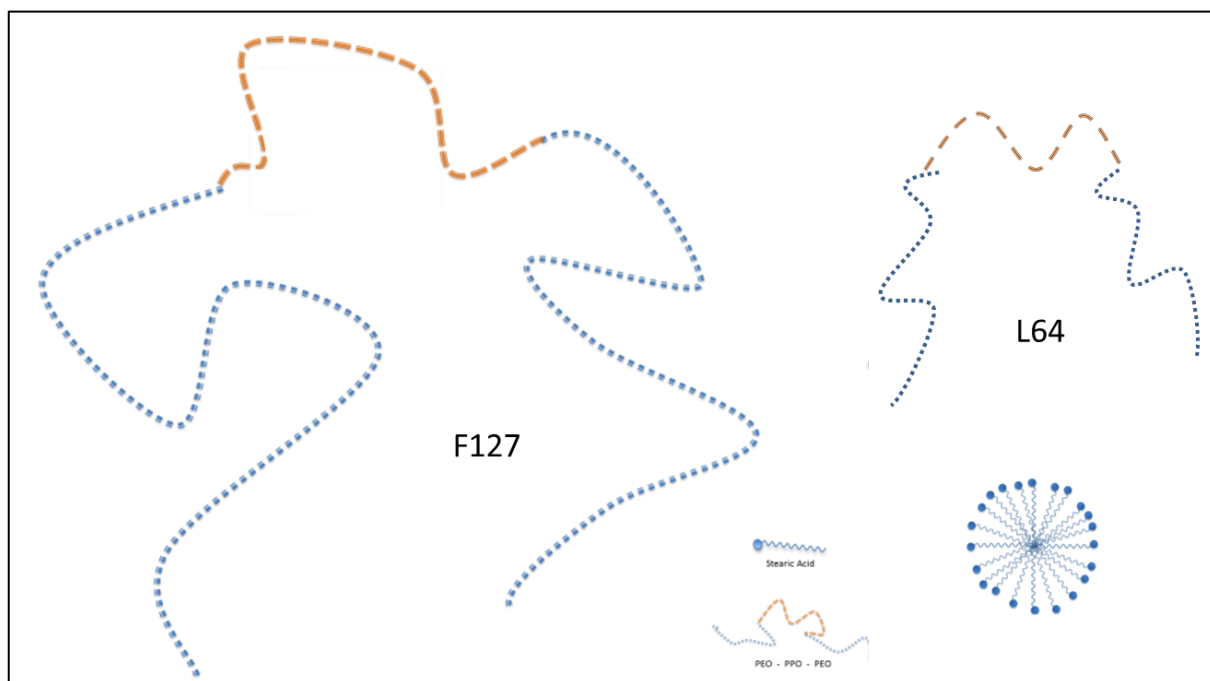


Figure 4.4.2 Pluronic® F127 molecule and a stearic acid micelle. Drawn to scale to emphasize the difference in size and why CMC is lower for larger molecules.

L64 is a relatively hydrophobic poloxamer with 40% hydrophile, F127 is predominately hydrophilic with 70% hydrophile and stearic acid is a simple surfactant with a singular hydrophobic head and hydrophilic tail.

Under dynamic conditions simple surfactant molecule (such as stearic acid) can move easily in solution and surface agitation has a minimal effect on the surface tension value. The Pluronics® shown in Figure 4.4.2 are much larger molecules than the simple surfactants and large molecules are cumbersome and move slower when in solution. This means that increased surface agitation causes a greater effect to the surface tension value.

The data in Figure 4.2.1.1 to Figure 4.2.1.5 compliments the literature and increased surface agitation shows an increase in the surface tension. It is also clear from the figures that concentration, size and hydrophobicity are all influential to the surface tension behaviour.

The dynamic surface tension data also highlights how molecular weight and hydrophobicity affect molecule mobility. Hydrophilic Pluronics® and Tetronics® such as F127 show a greater increase in surface tension over increased agitation speed. At the highest bubble speed all but one of the hydrophilic surfactants has a surface tension above 60mN/m. This is not the case for hydrophobic surfactants such as 1304. The surface tension does increase with agitation but at a much lower rate, with the highest surface tension value being just above 50mN/m. Figure 4.2.1.7 shows the dynamic surface tension gradients against surfactant molecular weight. This is important as it takes in account surface tension change rather than data values. As expected the hydrophobic surfactants have low gradients, change less with agitation. As previously discussed a surfactant needs to successfully reduce the surface tension to remove dirt from a surface. The eye and cleaning are dynamic processes; if a surfactant cannot keep the surface tension low under dynamic conditions then its ability to clean will be poor.

As with many things regarding contact lenses, there is a compromise. Here it is between in-eye comfort and cleaning efficiency. For this reason many contact lens care solutions contain a combination of surfactants. The purpose of one surfactant is to clean and one to condition and coat the lens. The combination of surfactants in a solution leads to surface tension changes. When the static surface tension is measured, both surfactants contribute to the overall surface tension value. However, when the surface tension is measured under dynamic conditions, it is the behaviour of the smaller molecular weight surfactant that is dominant. This is because the small molecules are more able to move about and return to the surface than the large molecules.

MPS data presented in Figure 4.2.2.3 shows how the addition of a small surfactant can affect the dynamic behaviour. Both Opti-Free® solutions contain Tetronic® 1304; RepleniSH has added ethylenediamine tri acetic acid which is a low molecular weight surfactant. The dynamic data clearly shows that the surface tension of RepleniSH is less affected by increased agitation.

In Chapter 1 the phenomenon of surface tension has been discussed, together with methods of its determination and its importance in cleaning. The principles of cleaning are reproduced above to underline the importance of surface tension changes with concentration. The critical micelle concentration represents the point at which the increase in surfactant concentration no longer causes the progressive decrease in surface tension which characterises the surface tension prior to the CMC (see Figure 4.3.1). The CMC indicates that the molecules are no longer congregating at the surface but are able to form into organised structures (micelles), where the hydrophobic parts of the molecule face inwards. Micelles are important in cleaning because they surround the dirt and debris and lift it from the surface and this is why the FDA requires MPSs to contain surfactant at a least its CMC [140]. Figure 4.4.2 shows stearic acid in a micelle formation (there needs to be many molecules present in order to form a micelle). Pluronics® and Tetronics® can curl and coil with each other. They do not need as many molecules to form micelles and will have a lower CMC value. Hydrophilic Pluronics® and Tetronics® have the added hindrance of long PEO 'arms'. At high concentrations these long 'arm' chains could become entangled and this will reduce their movement in solution further.

There is a clear inflection seen at the CMC point in Figure 4.3.1. The FDA requires the surfactant to be at or above its CMC and the standard methodology for determination of the CMC of a surfactant is by surface tension measurements over a range of concentrations[102]. The CMC approach is suitable for simple surfactants as micelles are required for cleaning to occur. This is not necessarily the case for large triblock copolymer surfactants, such as the Pluronics® and Tetronics®. The CMC data for these surfactants does not show a clear inflection point (see Figure 4.3.2). This has also been shown in the literature for other Tetronics® (see Figure 4.4.3). The large molecules have more complex behaviour and may even be able to coil within themselves and form mono molecular micelles.

As the surfactant concentration continues the increase, the surface tension for some surfactants (Pluronic® F127 Figure 4.4.3 and poloxamine 188 Figure 4.3.2) starts to increase.



Figure 4.4.3 Variation in surface tension with concentration (log scale) for 3 Tetronics®(304, 904 and 1307 plus Pluronic® 127) (13)

This phenomenon is caused by the hydrophilic chains of the molecules becoming entangled (hydrophilic entanglement). The molecules are then less able to move about and get to the surface; this would result in an increase of the surface tension value.

Figure 4.3.1 also shows the level of detergency as concentration increases. Above the CMC there is no increase in detergency, so increased surfactant concentration (above the CMC) does not improve the MPS cleaning ability. Although this thesis relates to the cleaning capability, it is not concerned with direct measurement of cleaning capability. However, it is important to make some general observations in relations to cleaning data obtained elsewhere (BCLA 2013 Conference Poster see Appendix)

Figure 4.4.4 provides the relevant information showing that the commercial MPS studied vary in lipid removal capability, that total lipid cleaning efficiency(residual surface fluorescence)[73] lies between 80% and 95% and in no case is all the sorbed lipid removed, but that all MPS are much more effective than saline.

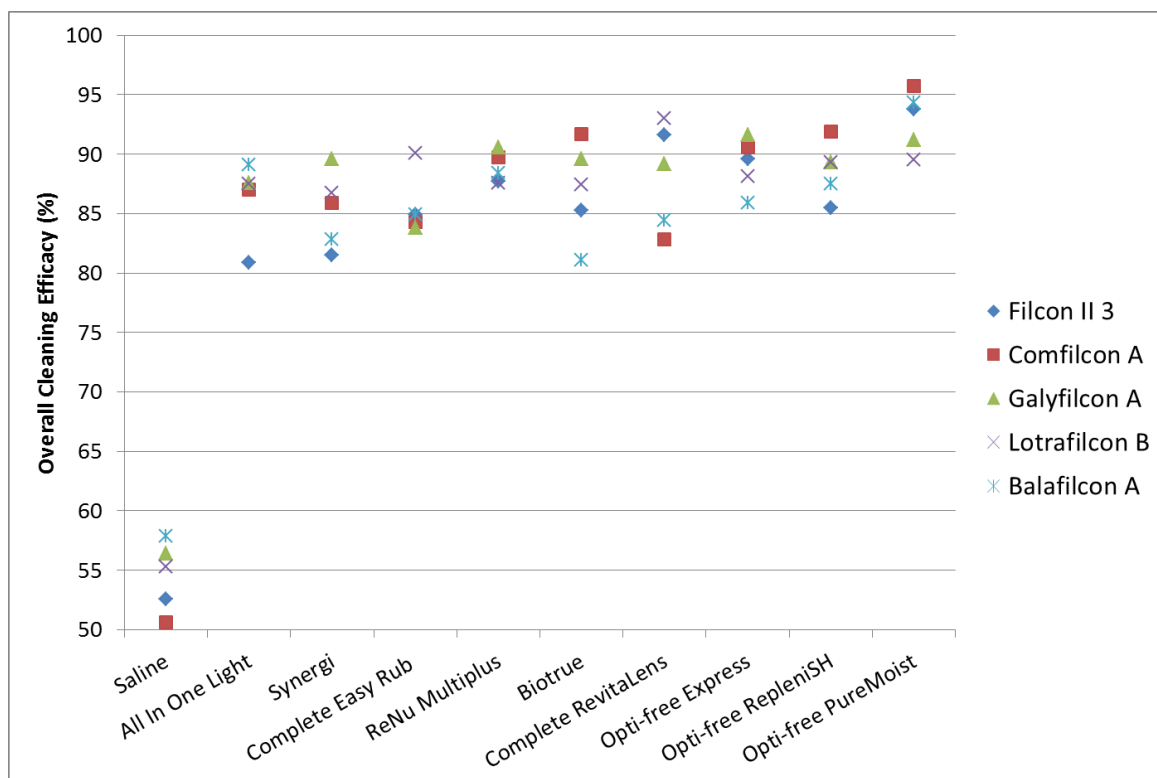


Figure 4.4.4 Overall Cleaning efficiency of several commercially available MPS in combination with several contact lens materials[147]

It is also important to note that cleaning efficiency shows material dependence and also decreases with duration of wear and progressive diffusion of lipids into the lens matrix [147].

Figure 4.4.5 shows the average cleaning efficiency from the data presented in Figure 4.4.4 and the static surface tension of the solution.

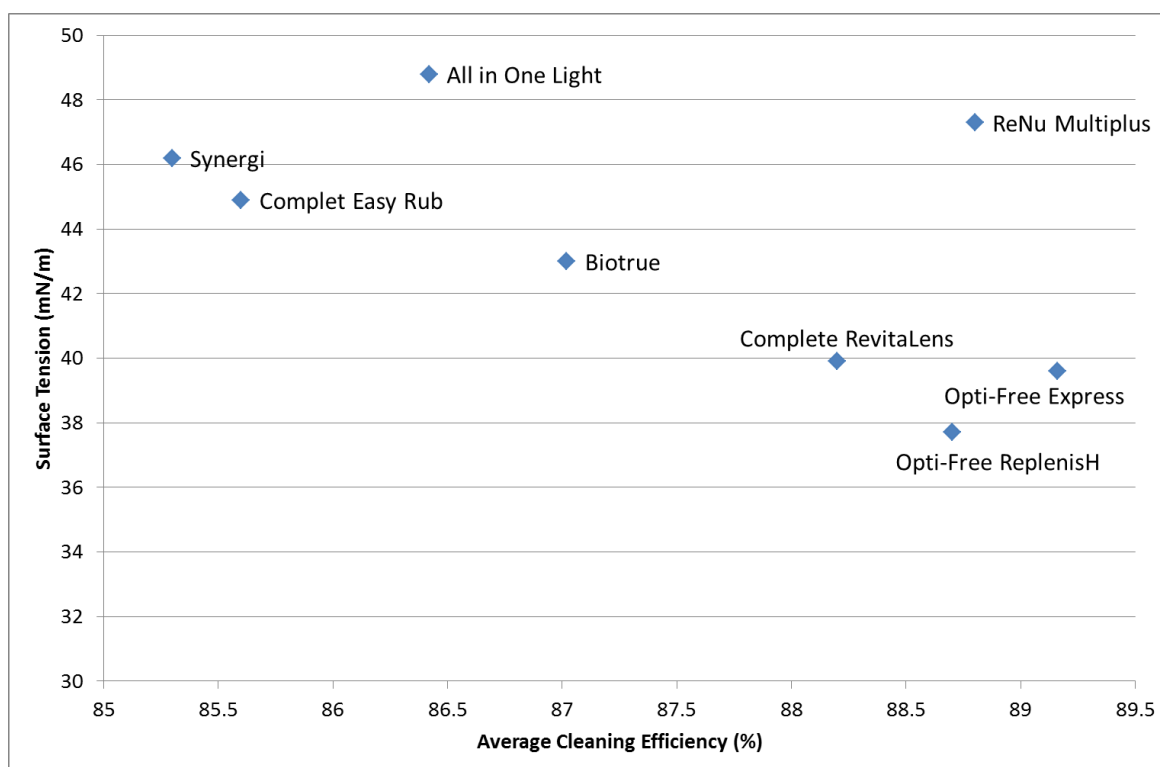


Figure 4.4.5 Static surface tension vs. average cleaning efficiency-an average value from a range of contact lens materials*

*Materials used were Filcon II 3, comfilcon A, galyfilcon A and lotrafilcon B

The multi-purpose solutions with the lowest static surface tension have the best cleaning efficiency. This may be due to an increased surfactant concentration in the better solutions, although an increase in surfactant does not lead to improved detergency (above the CMC). All in One Light® and ReNu® Multiplus perform better than expected in relation to their static surface tension. The surfactant size and hydrophobicity have been shown to affect the surfactant behaviour so this will also influence the cleaning behaviour. None of the MPSs are outstanding at cleaning (80-90% cleaning efficiency), but as declared several times, compromises are needed for the MPS to be an 'all-in-one' solution.

Statistical analysis showed that there was a poor correlation between static surface tension and average cleaning efficiency (-0.2). However, as a result of the small amount of data, this is not shown to be significant.

CMC values are not good single parameter predictors of MPS cleaning capability but surface tension (particularly dynamic) gives a strong indication of surfactant behaviour.

Surfactants from different commercial sources can be compared using the dynamic surface tension CMC measurements. Figure 4.2.1.3 and Figure 4.3.2 show data for poloxamer 188. Pluronic® F68If is poloxamer 188 supplied by BASF®, the other poloxamer 188 is supplied by an unknown manufacturer. There are clear differences between the dynamic behaviour and CMC curves. When a chemical is purchased the average molecular weight is often given. These surfactants are difficult to make and are made with different degrees of precision. The standard deviation of molecular weight can differ from company to company. The behaviour of the surfactant is a function of its molecular weight. The molecular weight is heterogeneous and different manufacturers' works to different degrees of precision. This discrepancy may go unnoticed during static surface tension measurements as all the molecules attribute to the whole value. The dynamic measurements, however, reflect the behaviour of the smallest surfactant in the solution. The product differences will manifest in the dynamic surface tension results.

The static measurements are influenced mostly by surfactant concentration and there is little distinction between the molecular weight and hydrophilicity of the surfactant. All surface active agents in a solution contributed to the static surface tension value.

The dynamic surface tension adds a further dimension; these measurements are influenced by both molecular weight and the hydrophilicity of the surfactant. When the surface is agitated, the large surfactants take longer to reach equilibrium, resulting in steeper plot gradients. The differences between the hydrophilic surfactants are more noticeable and as the agitation at the surface increases the data plots fan out. The more hydrophobic molecules evidently have a higher hydrophobic drive and want to get to the surface more than the hydrophilic molecules, and do so much quicker. Differences between surfactants contained in MPS are also seen in dynamic surface tension plots. This is clearly shown in Figure 4.2.2.3, where two solutions (Opti-Free® Express and Opti-Free® RepleniSH) have almost the same ingredients bar one low

molecular weight surface active additive in replenish. This additive has an obvious effect on the dynamic data plot, and while the surface tension for Express rises rapidly with bubble speed, Replenish maintains a low surface tension.

Dynamic surface tension highlights a difference between two surfactants that should be of the same molecular weight and hydrophobicity and in turn should behave the same. F68If and 188 are the same surfactant (poloxamer 188) from different suppliers. A range of molecular weights and hydrophobicities are contained in each surfactant, the surfactant name is an indication of the average values. The two poloxamers could contain a different range of molecules and this could be causing the differences in behaviour.

Although CMC clearly shows no direct correlation with cleaning efficiency as transitions are indistinct and do not show clear variation. Figure 4.1.1 collects static surface tension behaviour for a range of MPS which show some variation without great discrimination. Figure 4.2.2.3 shows a similar range of MPS studied with dynamic surface tension and here the variation with agitation shows good general correlation with cleaning performance.

These and other results show that cleaning capability and persistence increased (but not proportionately) with surfactant molecular weight: e.g. Tetronics 1304 > 904; Pluronic 127 > 87. Significantly, MPS surfactant concentrations do not always reflect the CMC of the parent surfactant but are influenced by the individual components included in the solution compositions. Cleaning capability of a MPS is not simply related to surfactant CMC, the static and dynamic surface tension measurements also provide useful predictive information.

At the outset of this chapter the point was made that the air/water interface is a surrogate for the contact lens/water interface. From the preliminary studies of the air/water interface, surfactant molecular weight, structure and hydrophobic ratio all influence molecule persistence at the surface. These variables should therefore also influence surfactant persistence at the contact lens/water interface.

Chapter Five

The Study of surfactant
release from contact lens
surfaces: Method
development
– Elution models

5. The Study of surfactant release from contact lens surfaces: Method development-Elution models

This chapter is concerned with establishing the methodology that will bring another useful set of experimental data to help in the understanding of the design of surfactant-based MPS for use in conjunction with contact lenses.

As chapter 4 has shown, surfactants differ in certain important respects. The use of the air/water interface as a surrogate gives an indication of surfactant behaviour at the contact lens surface; it allows for the surfactants to be put in a possible order in terms of mobility and hydrophobicity. However it does not demonstrate how much surfactant is retained at the surface, how much is removed through wear and how long it takes to remove all the surfactant. In the following chapter the lens material is an added variable; it is possible that different surfactants are more suited for different lens materials. Although it is known that surfactant molecules are removed from the surface during lens wear; the persistence at the surface is unknown, particularly for silicon hydrogels.

To measure on surfactant persistence at a lens surface it is necessary to develop an in vitro model of the ocular environment. This is because in vivo studies present too many variables in regards to on-lens surfactant persistence, tears contain many components that affect surface tension and modify the surface of a contact lens. It is impossible to distinguish between surfactants contained in the tears and those in the MPS or packing solution using surface tension measurements. So in-eye persistence models are not suitable here. Although in vivo study is the ultimate indicator of success, this work is concerned with establishing the structure property relationship to help in the design of potential systems for in vivo investigation.

An in vitro eye model is difficult to develop in practice because of the low volumes needed to mimic the natural system. In addition to this, in order to measure surface tension, a sufficiently large amount of liquid is needed. For a standard sized Du Noüy ring, this amount of liquid is approximately 10ml. There are other methods to measure concentration levels in small amounts of liquid, such as refractive index. Refractive index and surface tension methodologies were compared in section 4.3. and it was

determined that surface tension was the most sensitive property at low concentrations. Therefore the du Noüy ring methodology was chosen for sensitivity and convenience. There is no standard methodology in the literature to measure surfactant persistence on a contact lens. In order to create a model, compromises need to be made for certain variables (such as volume) it is not possible to precisely mimic actual tear volume.

5.1. In Vitro eye model and model evolution

As stated above, compromises need to be made in order to create an eye model and the first model presented here was designed to give initial comparative data. It was important to confirm that surface tension measurements would be a useful technique to show the removal of surfactant from the lens. Each subsequent model evolved from this basis with reduced volume and increased agitation. The aim is for the models to be as similar to the in-eye process as possible. Figure 5.1.1 shows the evolution process from the simplified in-eye volumes [148].

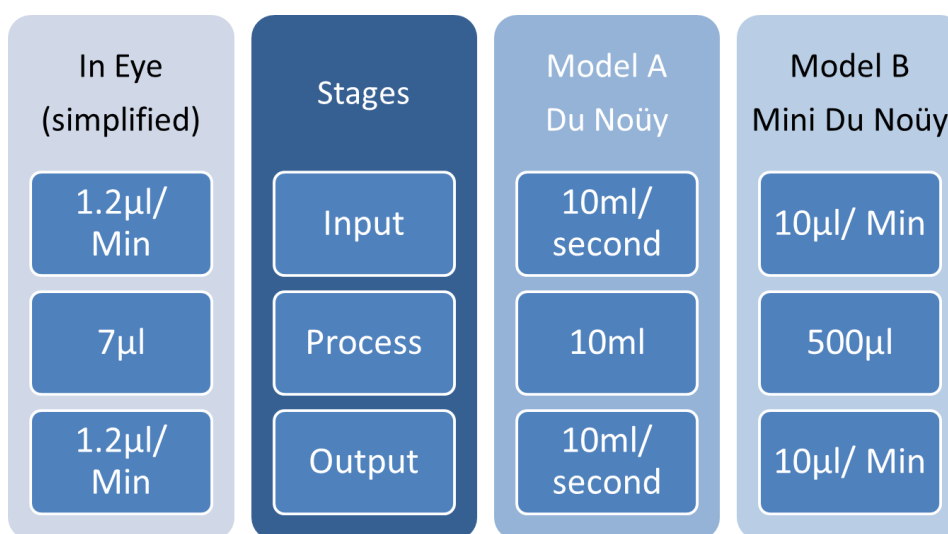


Figure 5.1.1 The experimental persistence models simplified into Input-Process-Output stages.

The eye models created here, aimed to be as similar to the natural eye system as possible and to compare persistence times of several surfactants used in many contact lens cleaning solutions. Prior to the persistence model experiments, the contact lenses were soaked in 1% surfactant solution (solutions and lenses shown in Chapter 2) for 24 hours. A single lens was used for each experimental run. In both models, differences

can be seen between the surfactant solutions used; conclusions can be made about which surfactants are more persistent at the surface. The surfactants used differed in both molecular weight and hydrophobicity. Chapter 4 concludes that both of these properties affect the persistence of the molecules at the surface.

5.1.1. The modification of contact lens surfaces using surfactants

This methodology applies only to contact lenses used in the surfactant persistence experiments. The contact lenses were treated as follows;

- Removed from the blister packs and packing solution
- Rinsed briefly with HPLC water
- Placed in a previously-made surfactant solution (1% Tetronic® or Pluronic®).
- The lenses were left in the solution for 24 hours to allow for sufficient surfactant uptake.

Several contact lens materials were used in the following experiments, including Clariti®, Clariti® 1Day, Acuvue® Advance® and Focus Dailies®. The data presented in previous chapters have shown that different surface properties are associated with different contact lenses. These surface properties may prove to be a factor in surfactant persistence. All lens analysis was repeated in triplicate.

Dehydrated lenses

Contact lens state of hydration prior to surfactant treatment was also introduced as a comparative variable in the persistence experiments. The lenses were prepared in the same way as they are prior to the sessile drop measurements;

- Microwave dehydration.
- The dehydrated lenses were then rehydrated in a 1% surfactant solution.
- The intention for this pre-treatment was to increase the surfactant persistence at the contact lens surface

5.1.2. Elution Model A – Large scale

This model was created as a starting point to provide a baseline of results, and from which all the other models were evolved. It also showed that surface tension measurements were viable. Within this model, 3 variations were arranged.

Figure 5.1.2.1 shows a simplistic schematic diagram of elution model A.



Figure 5.1.2.1 Schematic of Model A , Beakers containing 10ml of HPLC, a contact lens submerged in the first beaker and the lens path over the course of the experiment

All variations to Model A involved 10ml beakers. The agitation and soaking time was systematically changed to observe effect of the variation.

Variation 1 – combination model

The procedure involved 15 plastic beakers containing 10ml of HPLC water (see Figure 5.1.2.1) the contact lenses were pre-treated as previously described. The beakers were soaked and rinsed in hot water and rinsed again in HPLC water prior to each experimental run. This was to remove any remaining surfactant. A lens was placed into the water with plastic tweezers and left to soak for 4 minutes. After 4 minutes the lens was removed and placed into a new beaker of water (see Figure 5.1.2.1). This was repeated for the 15 beakers, for a total time of 1 hour.

Variation 2 – dipping model

This variation was developed to focus on the effect of agitation on surfactant removal (due to increased lens agitation). The experimental set up was identical to variation 1, only the lens soaking time was altered. Instead of 4 minutes, the lenses were placed in the water for approximately 1 second, removed straight away and placed in the next beaker of water. This was repeated for the 15 beakers.

Variation 3- soaking model

This variation was developed to focus on the surfactant removal due to desorption. The soaking times between variation 1 and variation 2 were reduced to increase lens agitation; to reduce agitation total soaking time was increased and the number of beakers reduced to two. Total experimental time was 1 hour. The lens was placed in the first beaker for 56 minutes, removed and placed in the second beaker for the remaining 4 minutes.

The contact lenses were disposed of after each experiment. A platinum du Noüy ring was used to measure the surface tension of the solution left in the beakers. Section 2.7.1 describes the methodology used.

Figure 5.1.2.2 shows the surface tension measurements of elutes from washed and unwashed Tetronic® treated contact lenses.

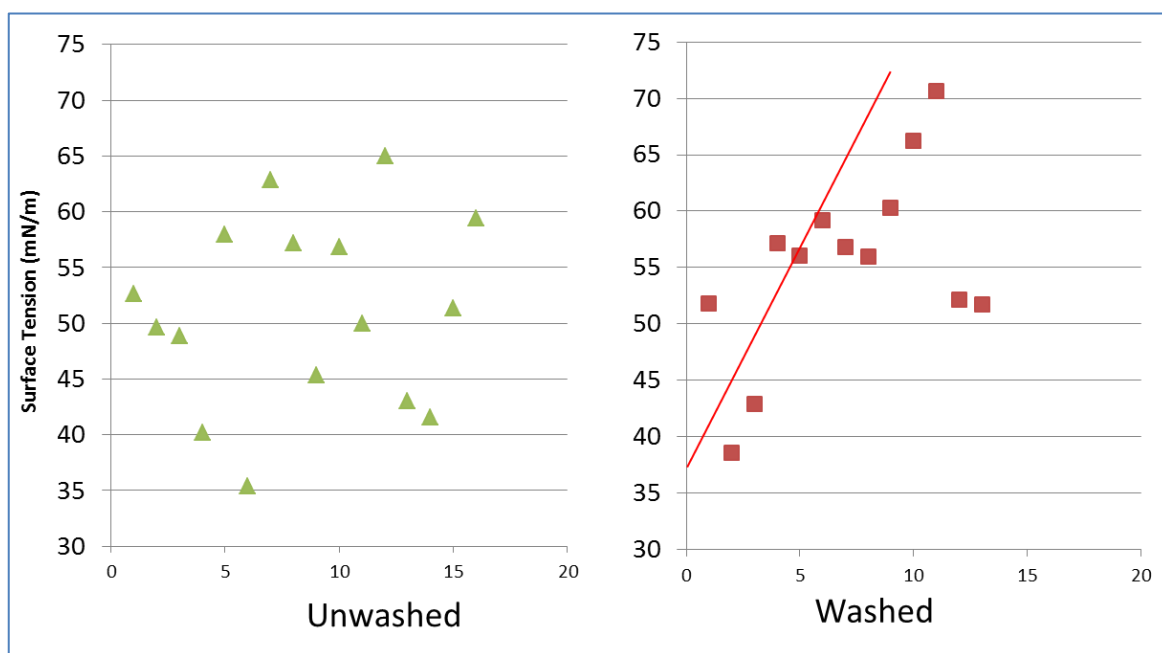


Figure 5.1.2.2 Tetronic® 1307 treated contact lenses. A comparison between surface tension measurements of elutes from washed and unwashed lenses.

The above graph compares 1307 treated lenses. One group of lenses were washed prior to the experiment and one group taken straight from surfactant solution. The purpose of Figure 5.1.2.2 was to select the experimental procedure. The surfactants that are being investigated in this work are found in many contact lens multi-purpose

solutions. These solutions are designed so there is no need for a rinsing step prior to lens insertion.

The unwashed lenses show very scattered data points with no obvious trend. If the lenses were left unwashed, 15 elutions would not be enough to show a steady surface tension increase. The washed lenses show a trend of increasing surface tension with each elution, less surfactant is removed after each elution (this implies that less surfactant is left attached to the lens surface after each elution). The washed lenses show more uniform surfactant elution than the unwashed lenses. Statistical analysis was carried out using the Pearsons Correlation, the R value for unwashed lenses is 0.0358, this is a very weak positive correlation and is not significant. The R value for washed lenses is 0.53, this is a moderate positive correlation, still not significant but a greater correlation than unwashed lenses. Therefore a washing step prior to each experiment was adopted.

5.1.3. Elution Model B – Small scale

The initial model A allowed for useful results to be gained, however the volumes used were much larger than the natural system. Elution model B was designed with reduced volumes. Table 5.1.3.1 states the specifications and limitations of the elutions models.

Table 5.1.3.1 In vitro eye model specifications and limitations

Model	Volume	Measurement	Comments
A	10ml	Standard	<ul style="list-style-type: none"> • Much larger volume than the tear film
		Du Noüy	<ul style="list-style-type: none"> • Experimentally simple to set up and measure surface tensions • Experiment duration 1-1.25 hrs • To investigate the viability of surface tension measurements • Reproducible results and simple to manipulate volume and agitation
B	500µl	Mini	<ul style="list-style-type: none"> • Still larger than the tear film volume
		Du Noüy	<ul style="list-style-type: none"> • 20x smaller than previous model • Experimental set up more complicated than previous model • Experiment duration 7-8hrs • Reproducible results • Surface tension measurements

Model A has much larger volumes than Model B, however the first model was a simple arrangement and only took 1-1.25 hours to complete.

The beakers from model A (10ml) were replaced with 1ml Eppendorfs (500µl) (see Figure 5.1.3.1). It was not practical to insert and remove the contact lenses as was done for Model A. Eppendorfs are much narrower than the beakers and the contact lenses would be continuously in contact with the sides of the Eppendorf and this contact would influence the surfactant removal.

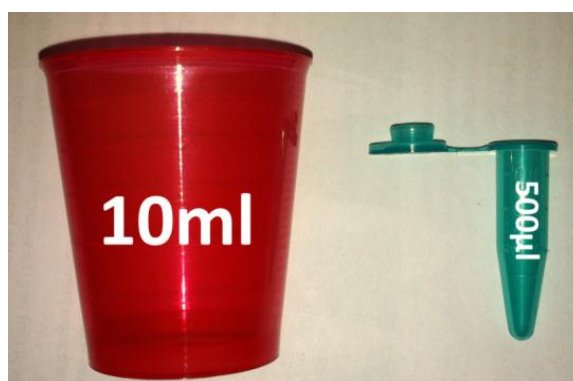


Figure 5.1.3.1 Beaker and Eppendorf comparative sizes

To allow for the lenses to remain in the Eppendorf for the duration of the experiment, an overflow and bund set-up was implemented.

It was possible for the whole contact lens (rolled, without sides touching) to be placed into the 1ml Eppendorf, underneath the 500 μl marker. Two overflow holes were made in the sides of the Eppendorf using a large needle, at the 500 μl point. This allowed for the lens to be completely submerged and for the solution to flow out steadily. The 1ml Eppendorf was then placed inside a 2.5ml Eppendorf to allow for the overflow to be collected as shown in Figure 5.1.3.2.

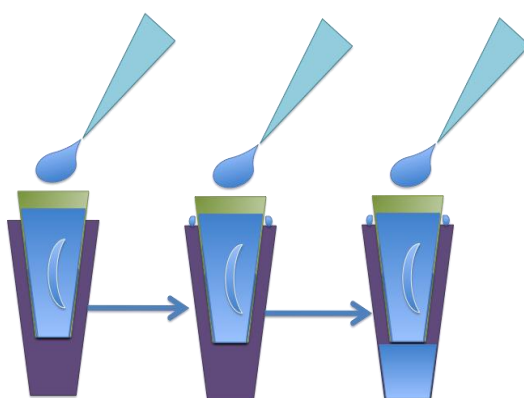


Figure 5.1.3.2 Schematic of the stages involved in Model B. Dispense, soak and overflow

All Eppendorfs were placed onto a shaker and continuously agitated. 500 μl of HPLC water was dispensed into the 1ml Eppendorf at the beginning of the experimental run ($T=0$) using a pipette, 100 μl of HPLC water was then added at ten minute intervals and the 2.5ml overflow Eppendorf was exchanged every hour for 8 hours. The small Du Noüy ring method (see section 2.7.2) was used to measure the surface tension of the collected overflow liquid (elutes). Lenses and elutes were disposed of after each experiment.

Chapter Six

Pluronic persistence:
Elution eye models and
surface tension data

6. Pluronic persistence – Elution eye models and surface tension data

As stated in Chapter 4 contact lens multi-purpose solutions contain surfactants, predominantly to clean the lens. The results presented in Chapter 3 show that the addition of surfactants to the packing solution does increase the initial lens wettability. Most contact lens wearers already use MPS as part of their care regime and it is logical to pursue additional advantages to their use. There is also no need to alter the material matrix; the surfactant adds a molecular layer to improve lubrication. This modification is not permanent and can be removed within a few minutes of contact lens wear. However, Chapter 4 shows that the structure of a surfactant effects the way in which it behaves, especially under dynamic conditions. Chapter 4 investigates surfactant persistence at the air/water interface, this chapter investigates surfactant persistence (specifically that of Tetronics®) at contact lens/ water interface. The surfactants that are being investigated in this work are found in many contact lens multi-purpose solutions. Results from the models described in Chapter 5 are presented here in addition to ex vivo data.

6.1. Surfactant persistence on contact lens materials

The intention of the experiments in this chapter is to study the interaction between contact lens materials. Tetronics® and Plurionics® with different structural variations will be used to treat the lenses. In order to investigate surfactant/material interaction in the ocular environment, eye-like in vitro models were created.

The large scale dip/soak model (Model A) has three variations; *combination* (variation 1) that consisted of 15 elutions and a soak time of 4 minutes, *dipping* (variation 2) that consisted of 15 elutions and a soak time of 1 second and *soaking* (variation 3) that consisted of 2 elutions and a total soak time of 1 hour. The surface tension of all elutes collected was measured in all experimental models.

The small scale elution model (Model B) was created to allow for lower sample volumes and flow rates (500µl volume and 10µl/minute flow rate). This model ran for a total of 8 hours and elutes were sampled every hour.

The surface tension of all elutes collected was measured for all experimental models (see Chapter 5).

The contact lenses were washed after surfactant treatment and prior to the persistence experimentation. Care regimes recommended for MPS do not state a rinse step, however washing the lenses provides less variable results (see Figure 5.1.2.2) and easier analysis of the data. The washing step can also represent reflex eye behaviour where increased tearing [64] and blink rate are experienced when lenses are initially inserted into the eye. This reflex behaviour will remove more surfactant than normal tearing and blinking.

The large scale combination model (Model A - Variation 1) was used to acquire the results in Figure 6.1.1. Clariti® monthly contact lenses were treated with 1% Tetronic® solutions for 24 hours. Clariti® lenses are the only European mass produced contact lenses currently on the market. In addition Sauflon, the company that produces Clariti®, contributed financially to this work and provided numerous lenses to study. The contact lenses were removed from the water after 4 minutes and the surface tension of the remaining water was measured. The surface tension measurements generally increase after each elution.

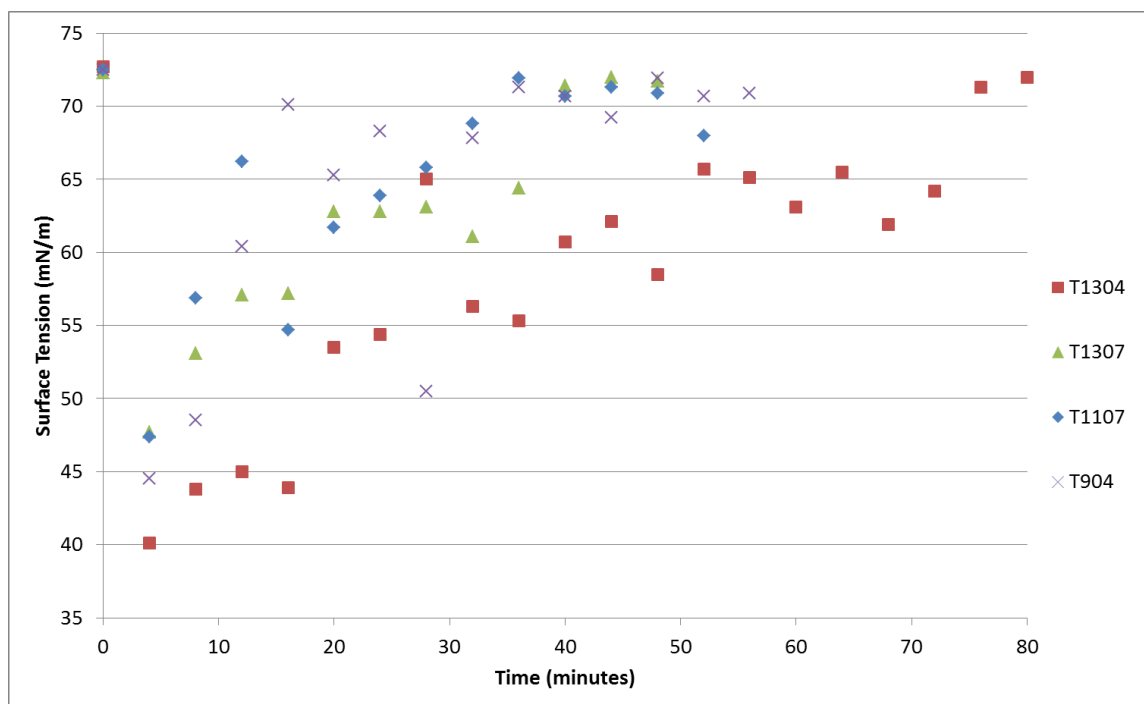


Figure 6.1.1 Tetronic® treated contact lenses. Tested using Model A, variation 1. A comparison between surface tension measurements for each Tetronic®

After 40 minutes (10 elutions) the surface tension data for Tetronics® 1307, 1107 and 904) reaches approximately 72mN/m (the surface tension of water is 72.8mN/m). Elutes from the Tetronic® 1304 treated lenses reach approximately 72.8 by 76minutes (19 elutions) nearly twice as long as the other Tetronics®.

From this model and variation the most persistent Tetronic® is 1304. Tetronics® 904, 1107 and 1307 behave very similarly in this experimental model. The dominating surfactant property here is molecular weight, as the larger molecule is the most persistent.

The large scale dipping model (Model A variation 2) was used with the same contact lens/ Tetronic® combinations. This model variation reduces the soak time from 4 minutes to approximately 1 second; this in turn increases the agitation at the surface of the lens. Surface tension measurements are taken of the remaining water after dipping and Figure 6.1.2 shows the recorded data from all elutes. The data points for all Tetronics® follow a very similar pattern and there are reduced differences between the data sets, nevertheless it is still possible to see differences.

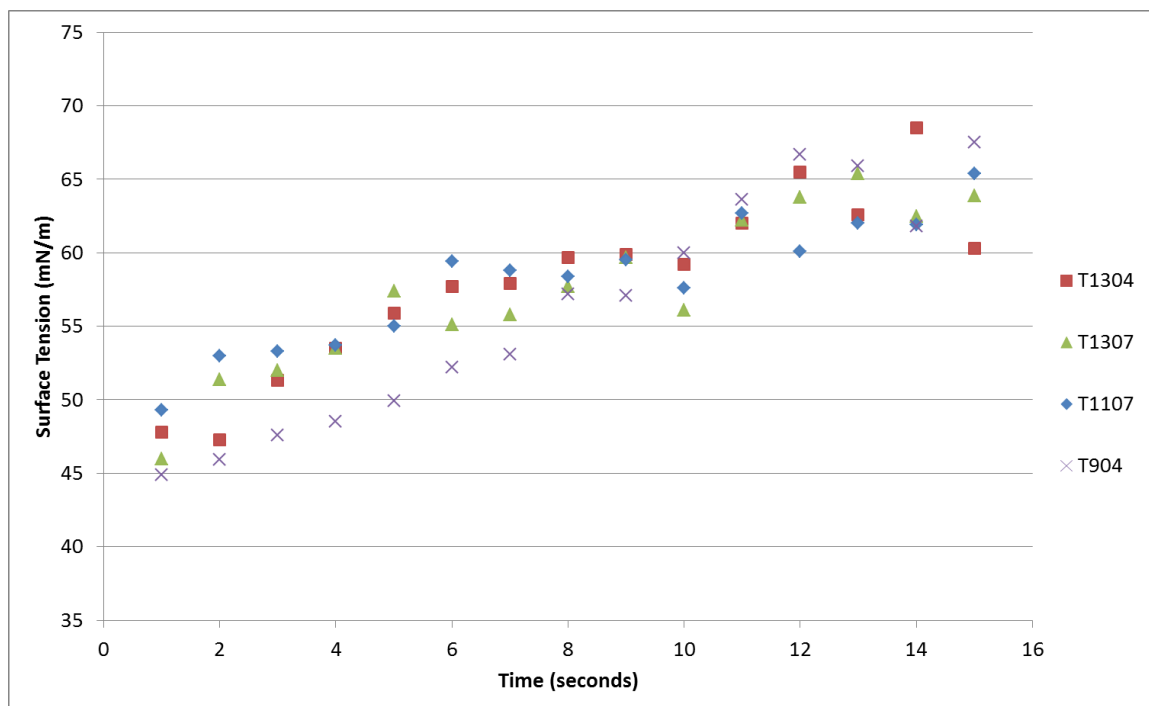


Figure 6.1.2 Tetronic® treated contact lenses. Tested using Model A, variation 2. A comparison between surface tension measurements for each Tetronic®

The most persistent Tetronic® is 1304 again, its starts to behave differently towards the end of the experiment. 904 shows the lowest surface tension values up to 10 elutes, the surface tension values then increase in line with the other Tetronics®. 1307 and 1107 behave very similarly to each other.

This variation highlights the fact that increased agitation reduces the differences between the Tetronics® and reduces the time that they are persistent at the lens surface. Tetronics® 1304 and 904 were most persistent in this model and variation, and the dominant surfactant property is molecule hydrophobicity (hydrophobic drive). Both of these Tetronics® consist of 40% polyethyleneoxide (PEO) and 60% polypropyleneoxide (PPO). PPO is mostly hydrophobic and this segment forms the hydrophobic centre of the molecule. The hydrophobic parts of the molecules are attracted to the hydrophobic domains on the lens surface. The results shown in Figure 6.1.1 and Figure 6.1.2 compliment the data presented in Chapter 4, where hydrophobic drive is one of the surfactant properties that influences the dynamic behaviour.

The large scale soaking model (Model A variation 3) also used the same contact lens/Tetronic® combinations. Here the soak time was increased to a combined total of 1 hour. The first soak lasted for 56 minutes and the second soak for 4 minutes. Figure 6.1.3 shows the surface tension values of elutes.

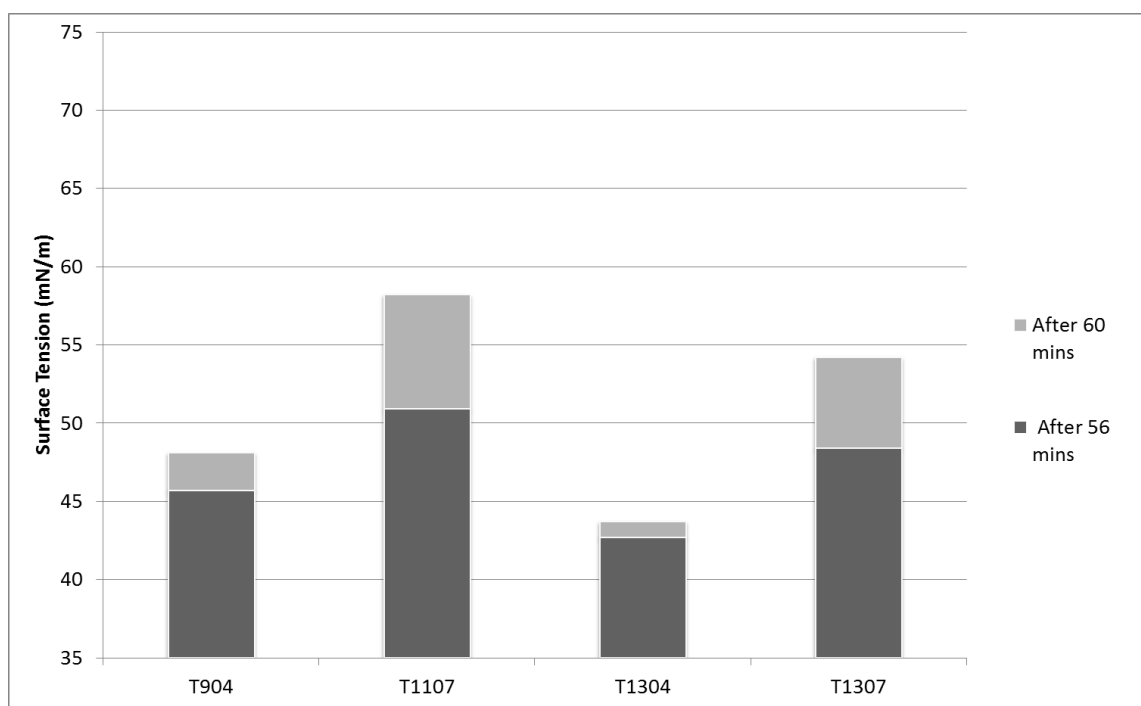


Figure 6.1.3 Tetronic® treated contact lenses. Tested using Model A, variation 3. A comparison between surface tension measurements for each Tetronic®

The surface tension of the first elutes show similar values to the first elutes from Figure 6.1.1 and Figure 6.1.2. This indicates that a similar amount of surfactant is being removed regardless of soak time. The second elute for the Tetronics® shown in Figure 6.1.3 seems to be influenced by both molecular weight and hydrophobicity. The hydrophobic Tetronics® 904 and 1304 show only a small difference between the first and second surface tension values (2.4 mN/m and 1 mN/m respectively), whereas the hydrophilic Tetronics® 1107 and 1307 have a greater difference (7.3 mN/m and 5.8 mN/m respectively). It is assumed that a small difference between the first and second elutes is linked to increased surface persistence. Tetronic® 1304 has the smallest difference, followed by 904, 1307 and 1107. Thus molecular weight also influences surfactant persistence. The large molecules have greater persistence in this model variation.

There is much consistency between the dynamic surface tension behaviour and the surfactant persistence. From Figure 6.1.1, Figure 6.1.2 and Figure 6.1.3 it is clear that molecular weight and hydrophobicity have an influence on contact lens surface persistence as they do on the dynamic surface tension (air surface persistence) plots presented in Chapter 4. The hydrophobic molecules attach to the contact lens surface

more effectively than the hydrophilic molecules and small molecules are removed/desorbed from the lens quicker than the large molecules.

As with the dynamic surface tension data, hydrophobic drive is the main influence in surfactant persistence.

6.2. Tetronic Persistence on dehydrated treated contact lens materials

In this section data from the large scale combination and the Small scale models are presented. Here, lenses referred to as 'hydrated' lenses were hydrated prior to surfactant treatment and those referred to as 'dehydrated' were dehydrated prior to surfactant treatment. This was done in order to investigate whether a dehydrated hydrogel material would attract or adsorb more surfactant molecules than a hydrated material and if in turn the increased surfactant would be more persistent at the surface.

Many contact lens materials have a hydration step during in the manufacturing process. The aim of this experiment was to see if replacing water with a surfactant solution, at this hydration step, would allow more surfactant molecules to attach to the surface of the lens. The Lenses were either taken straight from packing solution and soaked in 1% Tetronic® solution(as in previous experiments presented in this chapter) , or dehydrated prior to soaking in 1% Tetronic solution. (*Relative persistence is the difference between the surface tension of water and the measure surface tension of the elute.)

Figure 6.2.1 and Figure 6.2.2 show the relative persistence* of Tetronics® 904 and 1304 on Clariti® and Clariti® 1 day lenses.

The soak time in these experiments was increased to 5 minutes, to increase overall experiment duration. The procedure was the same as the large scale combination model. Figure 6.2.1 shows the difference between hydrated and dehydrated treated Clariti® contact lenses. The y-axis is relative surface tension (the difference from water 72.8mN/m).

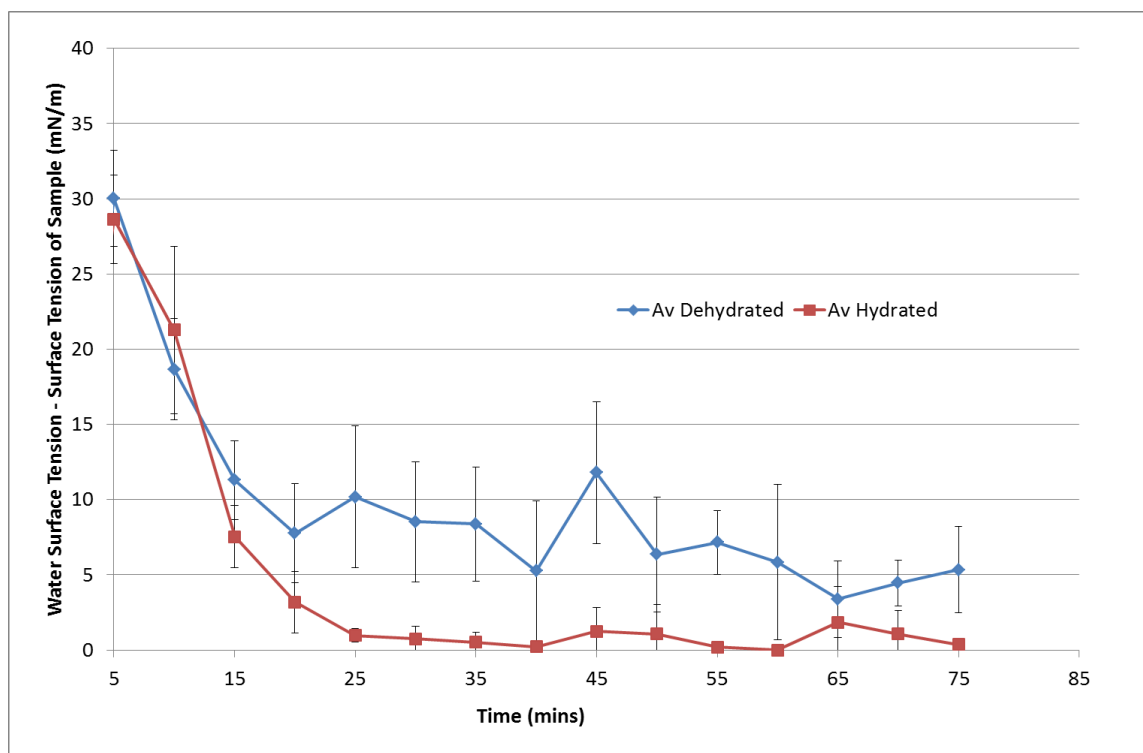


Figure 6.2.1 The surface tension changes over time of hydrated and dehydrated surfactant treated Clariti® and Clariti® 1 Day lenses. Average hydrated and Average Dehydrated relative persistence.

It is clear that there is a difference between the persistence on hydrated and dehydrated Clariti® lenses. The hydrated lenses plot drops to a very low relative persistence value at 25 minutes (5 elutions) in to the experiment. After this point the surface tensions of elutes are very similar to that of water. The data from the dehydrated lens elutes do not drop this low throughout the duration of the experiment. This indicates that there is still surfactant eluting from the surface of the lens. The pre-dehydrated lenses show increased surfactant persistence.

Figure 6.2.1 shows the average data from two contact lens materials (Clariti® and Clariti® 1 Day) treated with two Tetronics® (904 and 1304). In order to investigate the influence of these variables it is important to separate the data.

Figure 6.2.2 shows the relative persistence data of 904 and 1304 treated lenses separately.

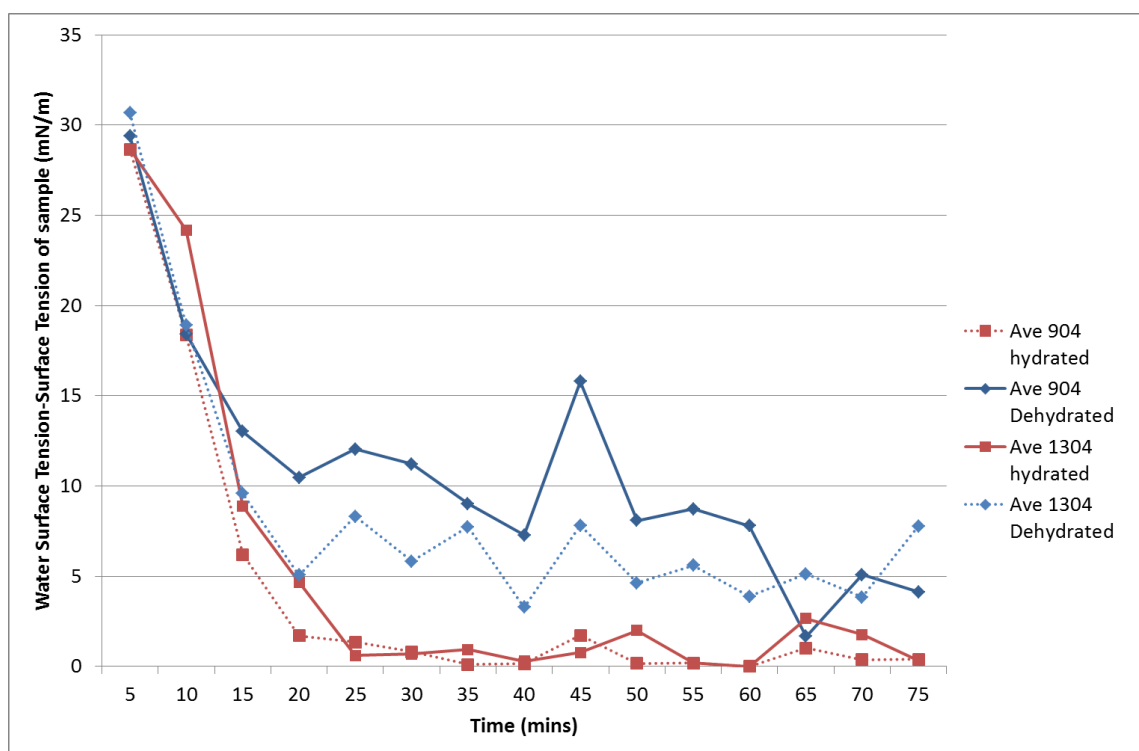


Figure 6.2.2 The surface tension changes over time of hydrated and dehydrated surfactant treat Clariti® and Clariti® 1 Day lenses. Average hydrated 904 & 1304, and Average Dehydrated 904 & 1304.

The dehydrated material treated with Tetronic® 904 shows the highest relative persistence value for most of the experiment and there is a distinction between the Tetronic® 904 and 1304 data sets. The 1304 data set shows steady persistence at the surface through the whole experiment. 904 has a higher relative persistence up until 65 minutes (13 elutions). The relative persistence seems to settle at a similar value to that of the 1304 data set. Elution 9 (45 minutes) shows an increase in relative persistence for both data sets. There is no external reason for this jump and so it remains unexplained.

The other variable in this experiment is contact lens material. Figure 6.2.3 shows the dehydrated water contact angles of Clariti® and Clariti® 1day lenses; the original lens with no surfactant treatment, after surfactant treatment/before persistence experiment, after persistence experiment (hydrated treatment) and after experiment (dehydrated treatment). This measurement was performed to see if any surface modification from the Tetronics® remained after the experiment was completed, even

if the surface tension values indicate there was no more surfactant being removed from the

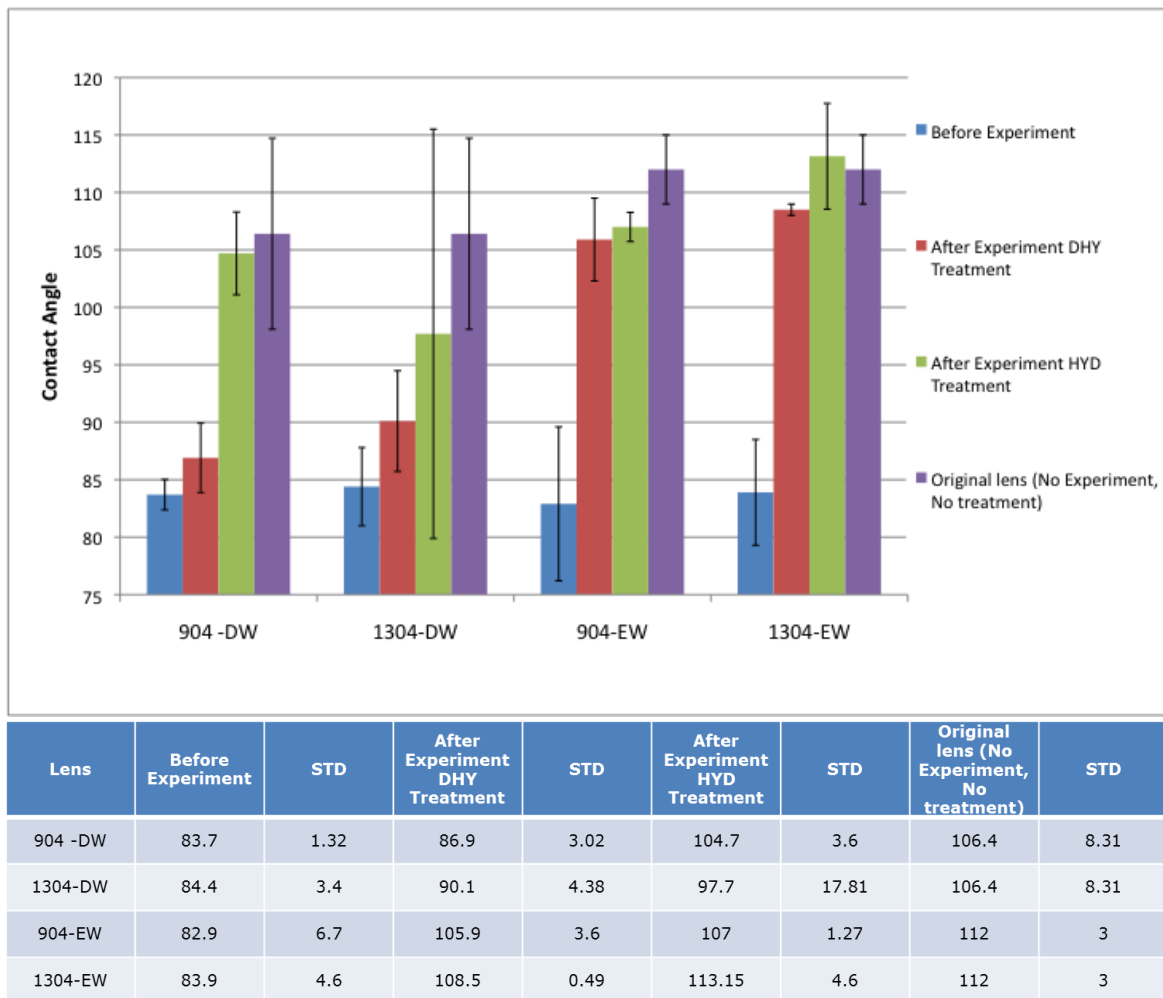


Figure 6.2.3 Water contact angles (sessile drop) of Clariti® (EW) and Clariti® 1day (DW) lenses, before and after the persistence experiment compared to the original lenses.

The first column in each category in Figure 6.2.3 is the modified contact lens before the experiment. There is a significant difference between the original lens (last column) and the modified lens (first column) for all lens/solution combinations.

The second column in each category in Figure 6.2.3 shows the water contact angles angle after persistence experiments for the contact lenses that were dehydrated and treated. All lens/solution combinations show the dehydrated lens contact angles are lower and significantly lower for Clariti® 1 day lenses.

All treated materials show lower contact angles for all categories except for Tetronic® 1304/Clariti® combination, this shows a slight increase in contact angle. In contrast 1304/Clariti® 1 day shows a notable decrease in contact angle. The 1 Day materials show a greater affinity for persistent surfactant surface modification. This difference could be the result of different manufacturing techniques between the monthly and 1 Day materials.

From these experiment data sets it would be favourable to rehydrate Clariti® and especially Clariti® 1 day materials in a surfactant solution to reduce water contact angles, increase surface wettability and possibly comfort.

6.2.1. Tetronic persistence on Acuvue® Advance® and Focus Dailies® contact lenses

The following experiments were completed in light of the positive conclusions of the previous results for treated dehydrated lenses. The small scale elution model (Model B) was used to obtain the data in this section. This model uses much smaller volumes, increase agitation and takes eight hours to complete. The mini Du Noüy ring (KRÜSS GmbH, Hamburg, Germany) technique was used to measure the surface tension of elutes. Lenses were removed from their blister packs and either dehydrated or left hydrated, they were then left to soak in surfactant solution for 24 hours. Tetronics® 904, 1107, 1304 and 1307 were chosen to treat the lenses. Acuvue® Advance® and Focus Dailies® materials were chosen because they have high and low water contact angles respectively (see Chapter 3).

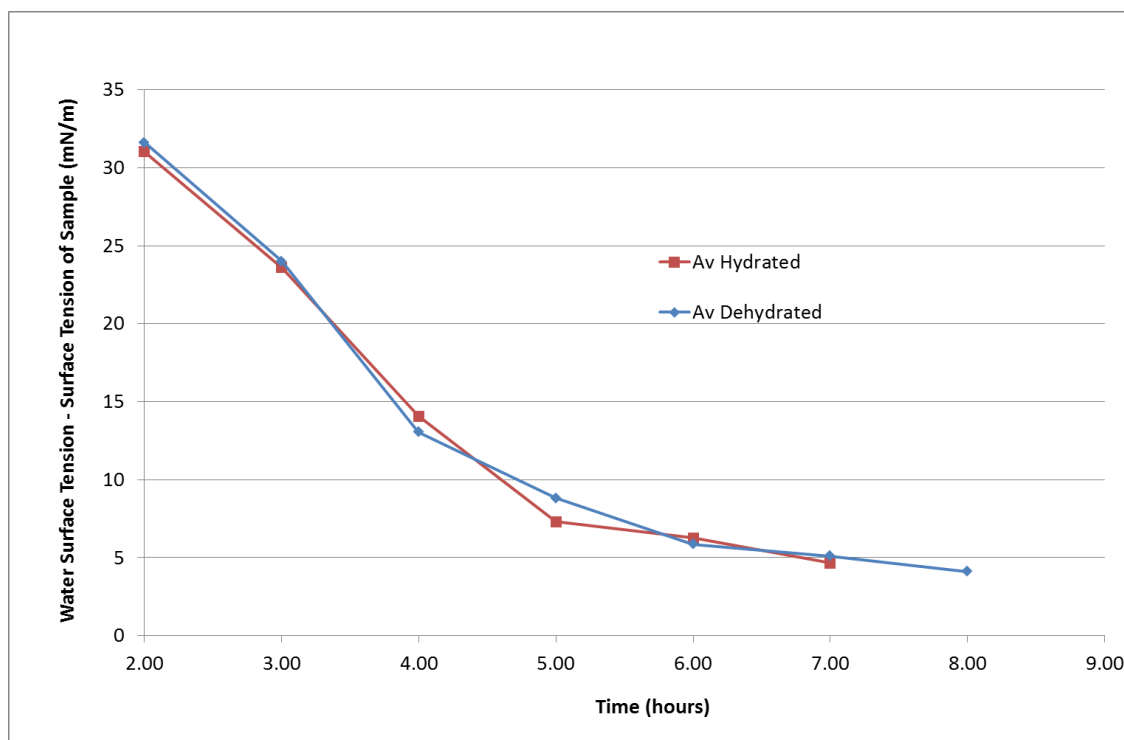


Figure 6.2.1.1 The relative persistence of Tetronics® on hydrated and dehydrated Focus Dailies® and Acuvue® Advance® contact lenses. Average hydrated and dehydrated results.

Figure 6.2.1.1 shows the relative persistence of Tetronics® on Focus Dailies® and Acuvue® Advance® lenses. The data presented is the average data for both lens materials and all Tetronics®. It is clear that dehydrating the lens prior to surfactant treatment had no effect in this case. Figure 6.2.1.2 shows the separate data for each lens material (further data is shown in Appendix 9.3). There is a slight difference between the relative persistence for the contact lens materials, with the treated hydrated Focus Dailies® showing the highest relative persistence. It is not a significant difference from either the dehydrated or Acuvue® Advance® data sets.

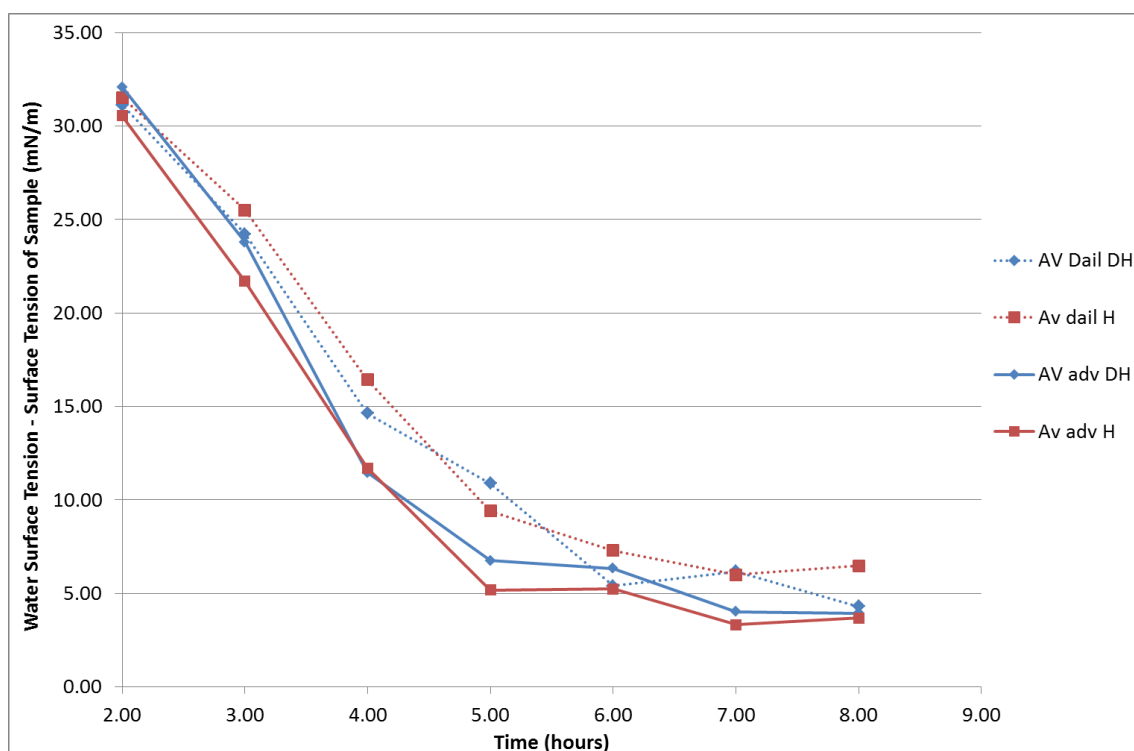


Figure 6.2.1.2 The relative persistence of Tetronics® on hydrated and dehydrated Focus Dailies® and Acuvue® Advance® contact lenses. Comparing the average Focus Dailies® and Acuvue® Advance® hydrated and Focus Dailies® and Acuvue® Advance® dehydrated results.

The dehydration of Clariti® materials pre surfactant treatment increases the surfactant persistence. This is because when the lenses are dehydrated emerging PVP collapses on to the surface and the surfactant has a greater chance of interacting with it. When the hydrated lens surface is treated all molecules have equal exposure to the surfactant.

The presence of PVP has also been shown to influence surfactant behaviour in other applications. PVP itself is not hydrophobically asymmetric and is not attracted to surfaces. The addition of PVP to a surfactant solution however, affects the surface tension and shifts the CMC value.

Figure 6.2.1.3 is included to show the effect of PVP on the behaviour of Pluronic® 127.



Figure 6.2.1.3 Dynamic surface tension of Pluronic® 127 vs concentration showing effect of added PVP

One of the key findings of this thesis stems from the fact that Clariti® materials differ in behaviour from other contact lenses even those that contain PVP such as Acuvue® Advance®.

Figure 6.2.1.4 shows the results from the dehydrated/hydrated lens experiments. Large scale combination model (Model A) with treated Clariti® lenses is shown with a solid line and small scale elution model (Model B) is shown with a dashed line. Hydrated lenses are shown with square markers and dehydrated lenses shown with diamond markers.

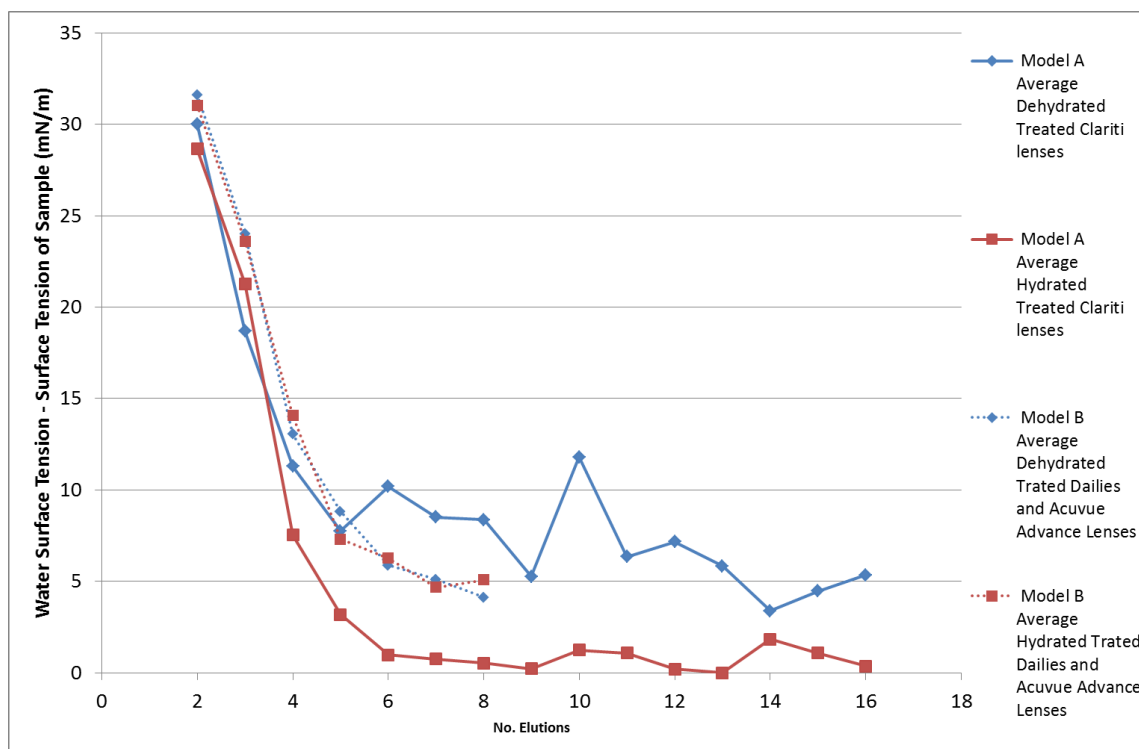


Figure 6.2.1.4: Figure 6.2.2and Figure 6.2.1.1 overlay. Method results comparison

Although the data are not strictly comparable because the flow rates used in the Clariti® experiment is 200 times greater than that used for the Focus Dailies® and Acuvue® Advance® experiment, it is interesting to see how both models compare. This graph is present here to highlight the effect each model has on the results. The data from the small scale elution model (dashed line) shows that the Focus Dailies® and Acuvue® Advance® lenses are still reducing the elute surface tension after 8 hours. This indicates that although there are no material or dehydration/hydration differences there is still surfactant coming from the lenses. Yet for the large scale combination model (solid line), after 75 minutes hydrated Clariti® is showing no surfactant removal. The results presented for the large scale model show that the increased flow reduces the surfactant persistence.

6.3. Ex vivo persistence experiments

The ex vivo study received prior ethics approval by the University Ethical committee at Aston University. Written informed consent from each subject to take part was obtained, once the requirements of the study had been explained[149]. Samples were collected from healthy volunteers with no history of ocular disease or disorder. An in

vitro experiment using the small scale elution model was conducted in parallel to the ex vivo experiment, in order to establish comparable data. Both ex vivo and in vitro experiments were prepared with Focus Monthly®, Soflens 1 Day® contact lenses and ReNu® multi-purpose solution. These materials and solution were used for two reasons; Etafilcon A (a charged material) has been used in other persistence studies [18, 41] and vilifilcon A (Focus Monthly®) is also a charge material. The Clariti® polymerisation reaction involves NVP monomer that is polymerised within the material matrix. Clariti® materials have shown increased persistence and this could be due to PVP leaching from the lens. To investigate the NVP effect in absence of charge Soflens 1 Day® (hilafilcon A) was used. Hilafilcon A also has vinyl pyrrolidone in the material matrix. ReNu® contains 1% poloxamines (Tetronic® 1107).

The in vitro experiment was conducted first to observe surface tension differences between the treated and untreated contact lenses. Treated lenses were soaked in ReNu® MPS for 24 hours and untreated lenses were soaked in saline for 24 hours. The small scale elution model was used to observe surface tension changes over four hours.

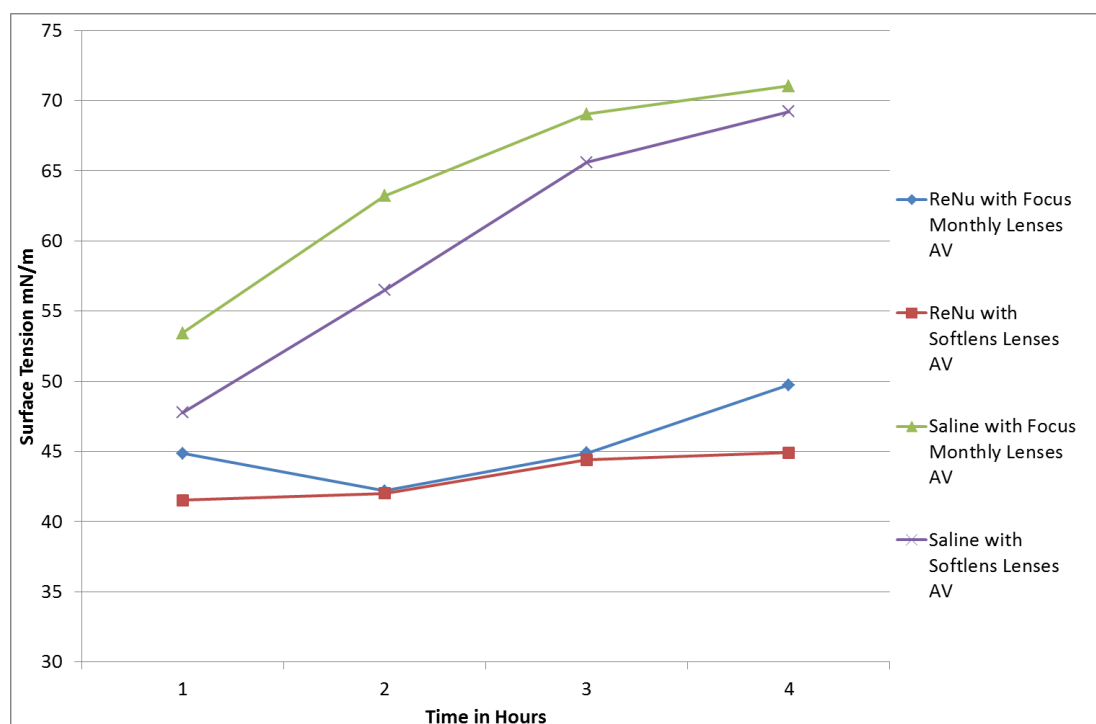


Figure 6.3.1 Surface tension changes over time of ReNu® and saline treated Soflens® and Focus Monthly® lenses in vitro.

Figure 6.3.1 shows the surface tension results of the eluents from ReNu® and saline treated Soflens and Focus Monthly® contact lenses.

There is a notable difference between the surface tension results from the ReNu® and saline soaked lenses. The saline soaked lenses show a progressive increase in surface tension (a decrease in surface activity). This indicates there is surfactant present in either the lens materials or packing solutions. The surfactant is more persistent with Soflens® material. After 4 hours there is almost no surfactant being removed from the surface of the contact lens. The ReNu® soaked lenses show a steady surface tension data set. The surface tension does start to increase as the experiment time increases; however the surface tension is still very low after 4 hours. Lower than the surface tension value for the initial saline measurement. Soflens® seems to retain surfactant longer than ® lenses, in both treated and untreated data plots. This could be a result of the PVP in the material matrix.

For the ex vivo experiment, contact lenses were taken from the packing solution and soaked overnight in a contact lens case. One lens soaked in ReNu® and one lens in saline. Lenses were worn by the subjects for designated times. After 1 hour of wear the lens was removed tested and disposed of, after 2 hours of wear the lens was removed, tested and disposed of, after 3 hours of wear the lens was removed, tested and disposed of, and so on. When the lenses were removed they were placed straight into a 1.5ml Eppendorf and 1ml HPLC water was added. The lens, water and Eppendorf were then placed on a vortex mixer for 30 seconds. The lens was removed and the surface tension of the eluent was measured to assess how much surfactant was still attached to the surface.

The following graphs show the ex vivo data for the same lenses that were worn by two subjects. Two lenses were collected from each participant (one for each eye) for each time slot. One lens was soaked in MPS prior to wear and the other soaked in saline.

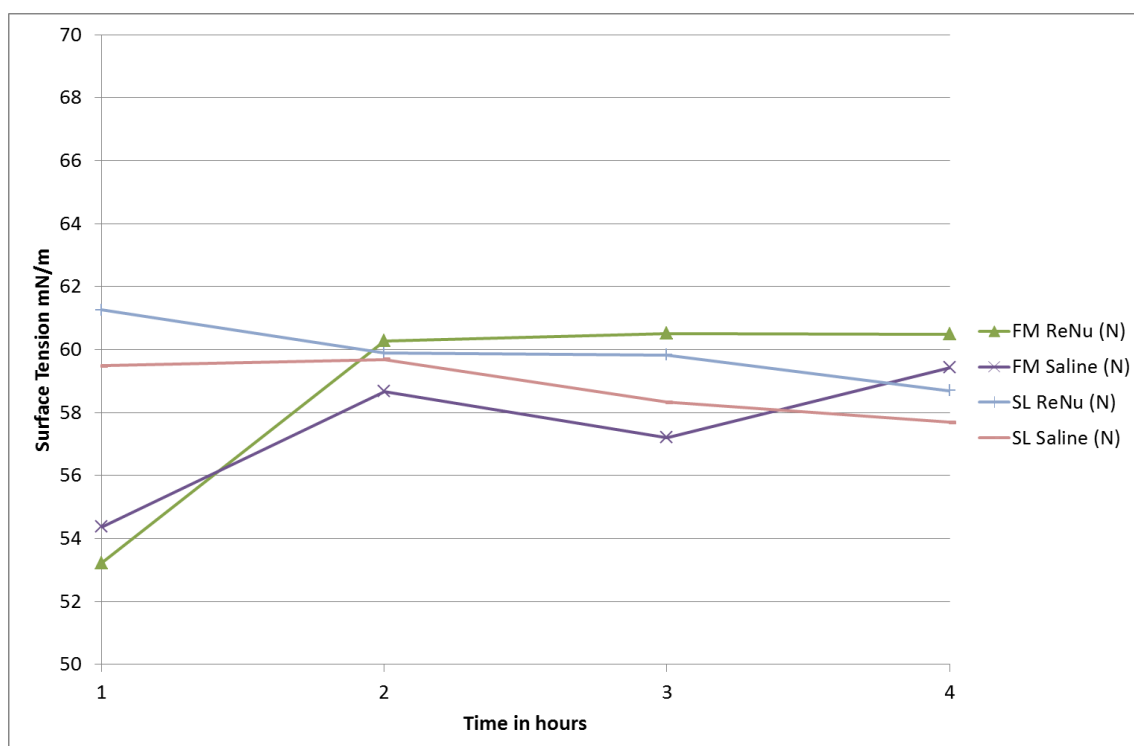


Figure 6.3.2 Ex vivo results for subject N. ReNu® and saline treated Soflens® and Focus Monthly® lenses.

Figure 6.3.2 shows the surface tension results for subject N. There is very little difference between the ReNu® and saline soaked lenses. After 1 hour wear time there is surface tension differences observed, this is influenced by the lens material. Focus Monthly®'s lenses show a lower surface tension eluent (more surface active) for the first hours of wear. The surface tension values are all very similar for the duration of the experiment. This could be a result of the ReNu® surfactant or a high concentration of surface-active molecules present in the tears.

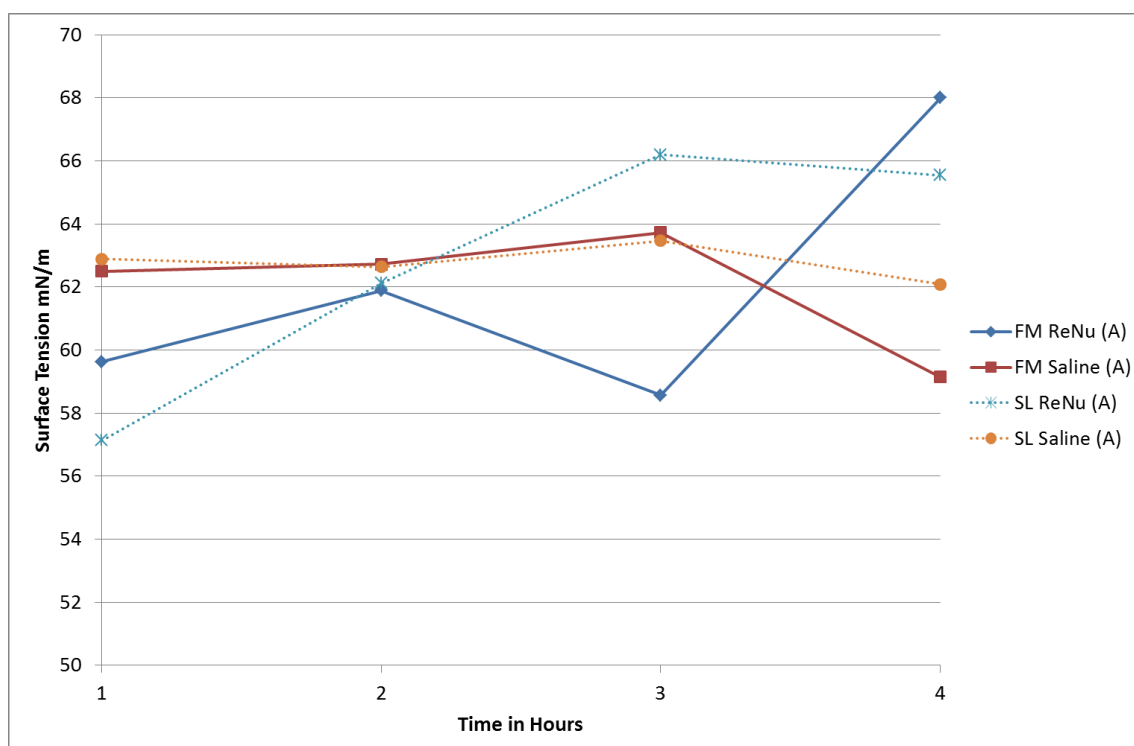


Figure 6.3.3 ex vivo results for subject A. ReNu® and saline treated Soflens® and Focus Monthly® lenses.

Figure 6.3.3 shows the surface tension results for subject A. The here shows a difference between the ReNu® and saline soaked lenses. The saline soaked lenses have a very steady surface tension data set, whereas the ReNu® soaked lenses have an increasing surface tension trend over time. The results from this subject have an increased range of surface tension values. The surface tension of eluent from ReNu® treated Focus Monthly® lenses after 4 hours wear is only 4 mN/m below the surface tension of HPLC water.

Subject N has very steady results throughout wear and subject A has much more varied results. This highlights how subject dependent ex vivo and clinic data can be.

Data from the in vitro models (Large scale and small scale elute models) indicates that higher flow rates and increased agitation removes surfactants from surfaces quicker. For ex vivo experiments this would relate to tear volume. This could be a possible explanation to the difference seen between the two subjects. It is possible to measure tear volume and flow rate using Schirmer strips as described in Chapter 2.9. The length of the Schirmer strip is 35mm. The time is measured while the strip absorbs the tears.

The time is recorded when 35mm is obtained or the wetted length measured after 5 minutes.

Table 6.3.1 shows the results from the Schirmer strip experiment.

Table 6.3.1 Schirmer strip results

Subject	Length (mm)	Time (mins)	Flow rate(mm/min)
A	35	2	17.5
N	26	5	5.2

The calculated tear flow rate for subject A is 17.5mm/min this is over three times larger than subject N (5.2mm/min). This indicates that subject A has more sensitive reflex reaction that produces a higher volume of tears when a foreign object is inserted into the eye. This data compliment the surface tension results in Figure 6.3.3. The saline surface tension results are very steady, so the saline is not causing and irritation to the eye. The ReNu[®] treated lenses have a low initial surface tension, indicating surface active molecules being removed from the surface of the lens. The surface tension rises in the continuing eluent to a near water surface tension. It appears that the tears are trying to wash off and dilute the solution.

High tear flow rates would also lead to a low concentration of tear components. Any tears present in the collected eluent would have a lower amount of surface active ingredients and consequently cause less of an effect to the surface tension value.

Subject N has a low tear flow rate and the surface tension of their tears do not change when either saline or ReNu[®] are used to treat the lenses. The tears present here may have a high concentration of natural surfactants that could be transferred to the lens surface and to the eluent.

The ex vivo surface tension results shown can be a result of the surfactants present in the ReNu[®] MPS or those naturally present in the tears. It is not possible to distinguish

between them with surface tension techniques. For this small sample size the tear flow rate is the controlling factor.

6.4. Discussion and Conclusion

Persistence differences can be seen between the surfactants for each experimental model presented in this chapter. The eye models evolved to reduce liquid volume, reduce the flow rates and to increase lens agitation. The initial model used 10ml beakers to represent the eye. The data collected from this model showed differences between the Tetronics® used and allowed for the following observations to be made. Molecular weight and hydrophobicity have an influence on Tetronic® persistence at the surface of a silicone hydrogel contact lens.

Model A has three variations that alter the soak time or agitation. In this model there are two mechanisms for removing surfactant from a contact lens; physical removal through agitation and adsorption to the soaking liquid. By altering the prominence of each mechanism it is possible to see which is most influential for surfactant removal. It was observed that increased agitation removed surfactant quicker and reduced the persistence differences seen between the Tetronics®. An increased soak time does not remove more surfactant, and shows more noticeable persistence differences between the Tetronics®.

For all variations of Model A, Tetronic 1304 showed the most persistence. This has been attributed to its high molecular weight and high hydrophobic drive that keeps it attached to the contact lens surface.

Ketelson et al also investigated Tetronic® persistence on etafilcon A contact lenses. The results presented in Figure 6.4.1 show differences between the Tetronics® used.

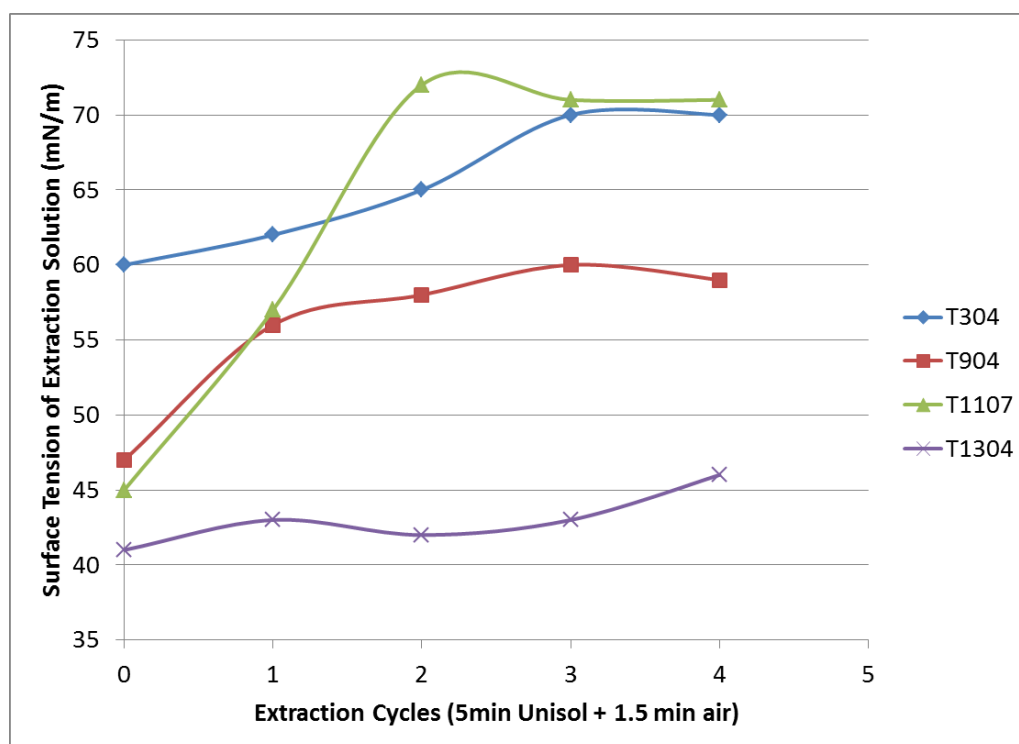


Figure 6.4.1 Surface tensions of extraction solutions from surfactant treated pHEMA-MAA lenses as a function of sequential cycles (adapted from)[41]

T1107, T304, T904 and T1304 have different persistence patterns. T1107 shows rapid elution whereas the hydrophobic T1304 seems to have a steady pattern of release. The interaction at the surface seems to be greater with higher molecular weight. This compliments the work present in this thesis as the hydrophobic drive is also the main influence for persistence. The volume used for the model used in the study is not stated, the soak time is 5 minutes and an air exposure time of 1.5 minutes is also included. The surface tension measurements are obtained through the Wilhelmy balance technique. The standard methodology for this technique requires similar liquid volumes to the standard du Noüy ring methodology and so can be likened to the large scale elution model. The lens material used in this study is a charged material; the materials presented in this thesis are more hydrophobic silicone hydrogels.

It is interesting that these results (Figure 6.4.1) have not been followed up and similar studies have not been done on silicone hydrogels. Given the proprietorial interests of the authors of T1304 the differences shown may not be so marked. That is certainly what has been observed in this thesis. The more recent publication from these authors

have tended to show/focus on the fact that enhanced persistence is seen with polyethyleneoxide-polybutyleneoxide block copolymers [150].

The large scale combination model was also used to investigate any persistence changes when lenses were dehydrated prior to surfactant treatment (see Figure 6.2.1). Tetronics® 904 and 1304 were used in this experiment to treat Clariti® and Clariti® 1 Day lenses. There was a clear difference between the relative persistence of the dehydrated and hydrated Clariti® and Clariti® 1 Day lenses. The dehydrated lenses show an increase in persistence because of increased exposure of hydrophobic domains at the surface. Acuvue® Advance® and Focus Dailies® lenses were chosen to further investigate surfactant persistence on dehydrated lenses (see Figure 6.2.1.1 and Figure 6.2.1.2). The data from this experiment shows no distinction between materials or surfactants used. Dehydrated Clariti® and Clariti® 1 Day show a greater affinity for surfactants, this indicates that the PVP that is released from Clariti® and Clariti® 1 Day lenses is assisting surfactant persistence. PVP has been shown to influence surfactant surface tension behaviour and CMC, PVP molecules are interacting with the surfactant molecules.. In addition to the surfactant present in elutes, the contact lens surfaces had also been modified. The water contact angles for all treated lenses were lower pre-experiment, and most showed lower contact angles post experiment. Dehydrated Clariti® 1Day lenses showed the most significant different from the original lens.

Other contact lens materials contain PVP in the material but different manufacturing methods are used. For example Acuvue® Advance® contains PVP as an internal wetting agent. Preformed High molecular weight PVP polymers are added to the material prior to polymerisation and the PVP is then released over time. The PVP leaching from the Clariti® materials can be of various molecular weights and may also contain silicone. The surface of Clariti® is unstable and continuously changing and deteriorating over time.

Tonge et al[18] assessed the ex vivo persistence of ReNu® MPS on etafilcon A lenses. A modified Wilhelmy plate methodology was used to gain contact angle data. The contact lens is cut into strips and used as a substitute Wilhelmy plate. The surface tension of the probe solution was measured after each experiment.

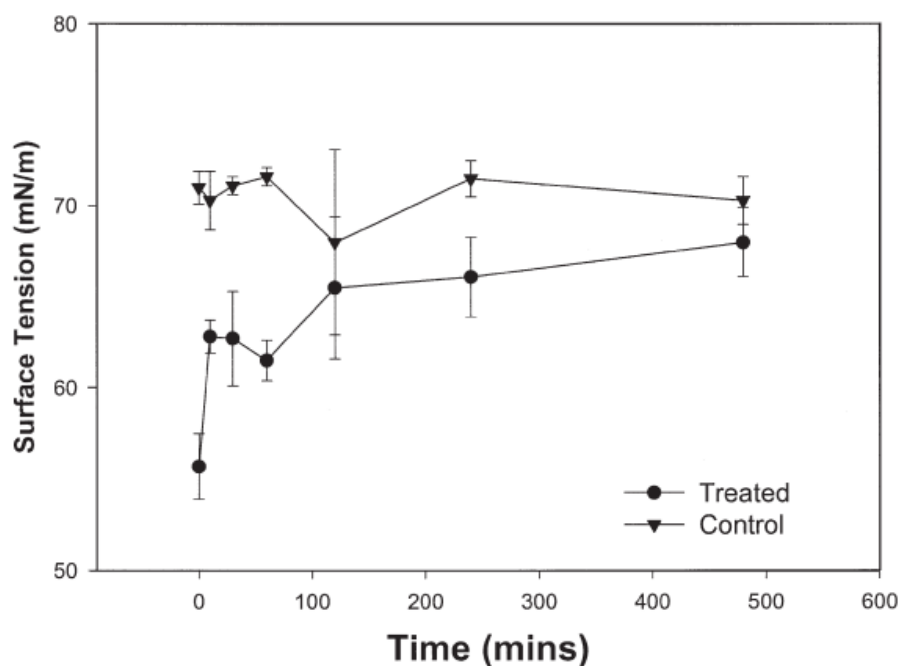


Figure 6.4.2 Surface tension of the probe fluid associated with treated and control lenses over time.[18]

Figure 6.4.2 shows a steady increase in surface tension over time. The surface tension data corresponds with an increase in advancing water contact angle over time.

The small scale elution model was used to assess the persistence of ReNu® on Focus Monthly® and Soflens 1 Day® contact lenses. Saline soaked lenses were used as a control and differences were noticed between the ReNu® soaked lenses and the control.

The principles were tested with two contact lens volunteer wearers, wearing their normal lenses and solutions in which the lenses were examined on removal from the eye. Half of the contact lenses were treated with ReNu® MPS in a similar way to the Tonge et al study. There were differences observed between lenses. However the controlling factor in these experiments was subject differences. The quantity of tears produced by each subject was different and this had an effect on the amount of surfactant removed and the concentration of surface active ingredients in the tears. The results in this chapter show that an increase in flow rate and agitation removes surfactant quicker than longer soak times and reduced flow rates. Subject A has a larger volume of tears and so washes the surfactant off quicker. These tears are also

less concentrated and would have a surface tension value closer to that of water (72.8.N/m). These data further illustrates how difficult an in vitro model would be to analyse. The overall results did show that the surface active ingredients in ReNu® can be persistent and for over 4hrs.

Chapter Seven

The Study of surfactant
release from contact lens
surfaces: Method
development
-Friction Model

7. The Study of surfactant release from contact lens surfaces: Method development-Friction model

To develop more effective in vitro models of the eye it is important to mimic the small volume of the tear film and the continuous agitation at the lens surface caused by lid movement. Measurement of coefficient of friction is a useful method to measure the behaviour of MPS as most contain polymers and surfactants to enhance surface lubrication. The Nano-scratch tester (CSM Instruments, Peseux ,Switzerland) (see section 2.8) is a technique that measures frictional forces and may allow for surfactant elution experiments with reduced liquid volumes. This chapter describes initial experiments that investigate this possibility. Because the work began at a late stage in the project only one material has been investigated.

For a standard friction measurement, 100 μ l of liquid is used as lubrication between the lens and substrate (see Figure 7.1). The standard friction program was modified and extended to run over 100 passes, instead of the usual 10. As there are so many data collected for each friction trace, the number of passes recorded was reduced. Runs 1,5,10,15,20...100 were recorded to reduce the amount of data to be analysed. The 100-pass friction program took approximately 2.5 hours to complete. The Nano-scratch tester (CSM Instruments, Peseux ,Switzerland) was prepared as described in section 2.8. The load and speed were kept the same (load 30 mN, speed 30 mm/min).

Figure 7.1 shows the experimental arrangement of the Nano-scratch tester.

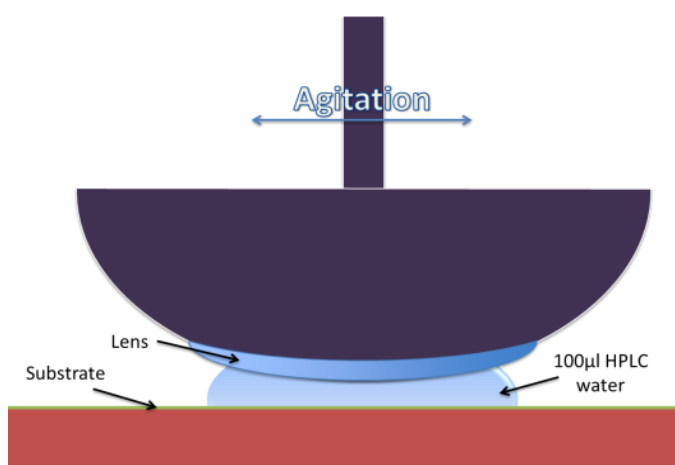


Figure 7.1 Schematic of Model C- Nano scratch tester (CSM Instruments, Peseux ,Switzerland) experimental arrangement

Lenses were either “treated” or “untreated” prior to the experiment. Treated lenses were removed from the packaging and soaked for 24 hours in a 1% Pluronic F127 solution; untreated lenses were taken directly from the packing solution.

All contact lenses were briefly washed and blotted before being placed on the mould. 100ul of HPLC water was used as the lubricant and silicone coated paper as the substrate as shown in Figure 7.1. This low surface energy substrate was chosen because it gives higher friction coefficients than the Melinex® film that is conventionally used, and thus shows greater differentiation between lens materials. The computer controlled program was started and continued until the 100 passes were completed. Initial experiments (no elution methodology) were left until completion without any external interference. For the elution methodology, after 10 minutes and every 10 minutes afterwards, the remaining lubricant was collected using a pipette (some of the original 100 µl water may be lost through evaporation) and was replaced by 100ul of fresh HPLC water. This had to be done quickly and carefully, as any force that touched the mould would appear on the friction trace. This elution/extraction cycle was repeated every ten minutes until the friction program was complete.

Table 7.1 shows the specifications and limitations of the two elution models described in chapter 6 together with the additional information for the friction model.

Table 7.1 Summary of the comparative Advantages and Disadvantages of In vitro eye models; Model A: large scale elution, Model B: Small scale elution, and Model C: Friction

Model	Volume	Measurement	Advantages/Disadvantages
Large Scale Elution A	10ml	Standard Du Noüy	<ul style="list-style-type: none"> • Much larger volume than the tear film (reduced sensitivity) • Experimentally simple to set up and measure surface tensions • Experiment duration 1-1.25 hours • Reproducible results and simple to manipulate volume and agitation
Small Scale Elution B	500µl	Mini Du Noüy	<ul style="list-style-type: none"> • 20x smaller than elution model A • Reduced volume but still greater than the tear film • Experimental set up more complicated than previous model • Experiment duration 7-8 hours • Reproducible results • Surface tension measurements
Friction	100µl-20µl	Nano-scratch tester (Friction)	<ul style="list-style-type: none"> • 5x smaller than model B • Friction traces used to measure persistence instead of surface tension values • Experimentally more complicated and required continuous observation

The initial intention was to measure the static surface tension of eluants collected from the HPLC water lubricant. However, in practice there was not enough liquid to obtain a measurement. The recorded friction traces did, however, show progressive differences over time and these traces proved to be a useful data source for this model.

7.1.Coefficient of Friction of Tetronic® treated contact lenses

The friction data presented in this section were obtained following the standard friction procedure that is described in Chapter 3. The Nano scratch tester (CSM Instruments, Peseux, Switzerland) records the frictional force produced when the substrate on a table moves horizontally in relation to the downward force from the mould and lens. From these force/distance traces the lubricity, coefficient of friction and stick slip values can be calculated. The instrument collects several hundred data points, relatively few of which are used on the plotted traces. The traces show accurate representation of the behaviour by direct observation, without the calculation absolute friction values. For this reason it is possible to directly overlay and compare friction traces of lenses that have been treated with different surfactants, such as those shown in Figure 7.1.2 and Figure 7.1.3, and to observe any differences in the mean COF and/or stick-slip behaviour.

In addition to the mean COF, stick-slip behaviour is important. This is not the variability about a mean value; 'stick' is the highest value and 'slip' is the lowest values (see Figure 7.1.1). The 'stick' is never increased with surfactant treatment and the maximum stick value is a useful indicator of relative surfactant effect. The degree of improvement is related to the structure of the surfactant (i.e. not all the surfactant treated lenses behave in the same way).

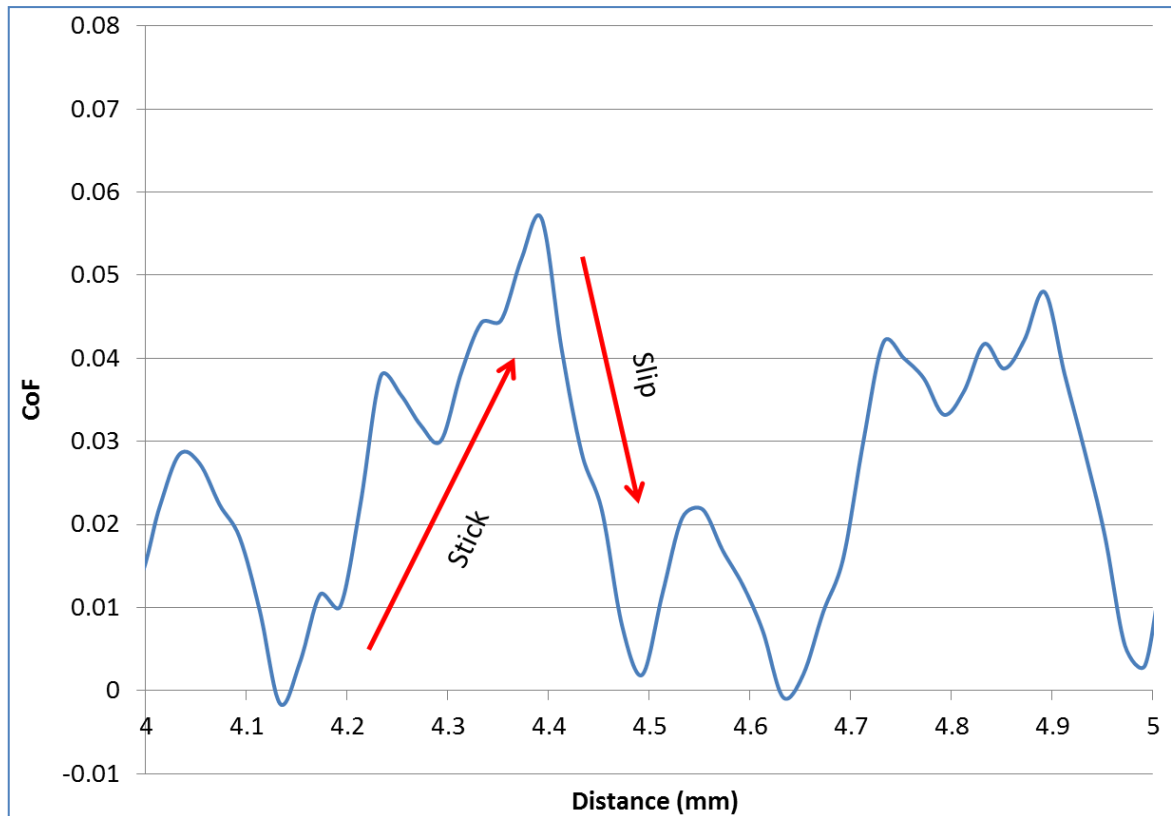


Figure 7.1.1 Slip and stick behaviour from a silicone hydrogel Coefficient of friction trace.

Slip stick behaviour may well influence the comfort of a contact lens, as a larger slip stick with similar COF would require a higher maximum force value. The stick slip however, is a second order interpretation and the COF is the most important.

Figure 7.1.2 shows the friction traces for untreated Clariti® monthly lenses in comparison to Clariti® lenses that have been treated with 1 % Tetronic® solutions. The traces for Tetronics® 1307 and 1304 treated lenses are included to show the hydrophobicity influence, and trace for Tetronics®1304 and 904 are included to show molecular weight influence. The COF technique enables us to compare the structure of surfactant, hydrophobicity and molecular weight.

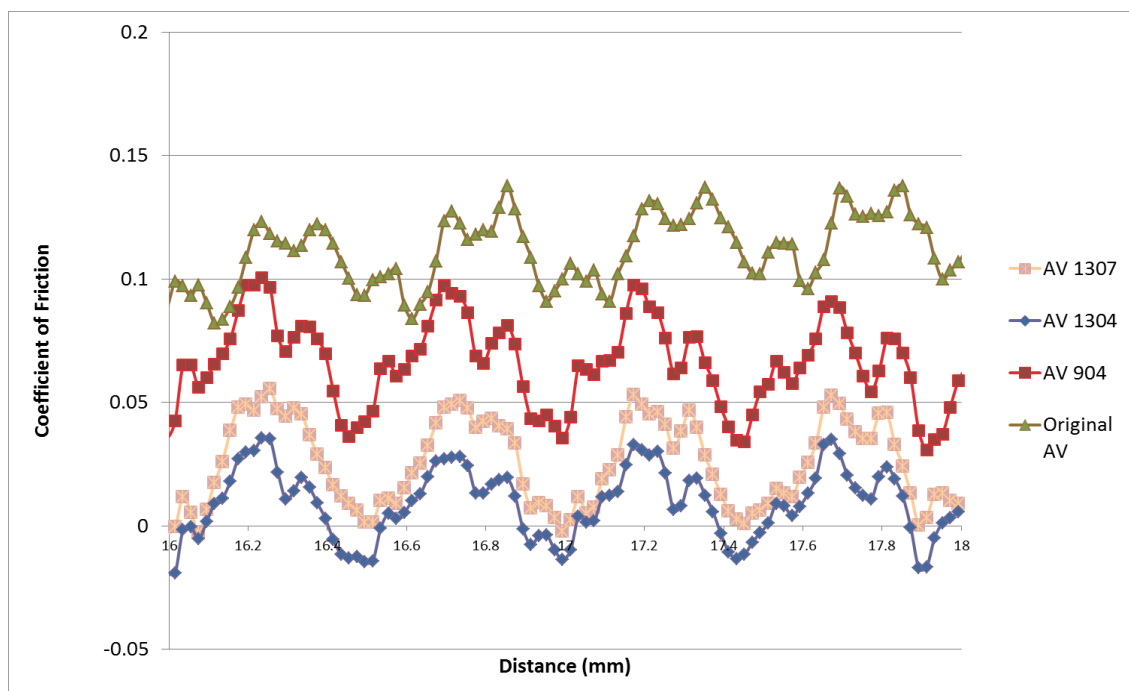


Figure 7.1.2 Coefficient traces for untreated and surfactant treated Clariti® monthly lenses

The traces for all the treated lenses fall below (lower frictional levels) those of the original lens, which might suggest that the surfactant molecules are desorbing from the treated lens surfaces into the HPLC water lubricant. This then reduces the coefficient of friction (COF). Alternatively the friction may be reduced by the surface-adsorption of the surfactant and in this case the friction will be higher as the surfactant undergoes desorption. The stick-slip patterns for the Tetronic® treated lenses are all similar, whereas the original lens shows a different pattern. The progressive increase on COF is where the contact lens material, lubricant and substrate are 'sticking' and displaying solid-like state behaviour (see Figure 7.1.1). The slip phase follows straight after and liquid-like behaviour is observed.

The Tetronic® that increases the lubricity (reduces friction) the most is 1304, closely followed by 1307 and then 904. The larger molecular weight Tetronics® are more effective in reducing friction. 1304 is more hydrophobic than 1307 so this could also be a factor. These data complement the results obtained from Models A and B and the result presented in Chapter 4.

Figure 7.1.3 shows the friction traces for Clariti® contact lenses treated with surfactant solutions Tetronic 1107, and 1307 solutions together with Pluronic 127.

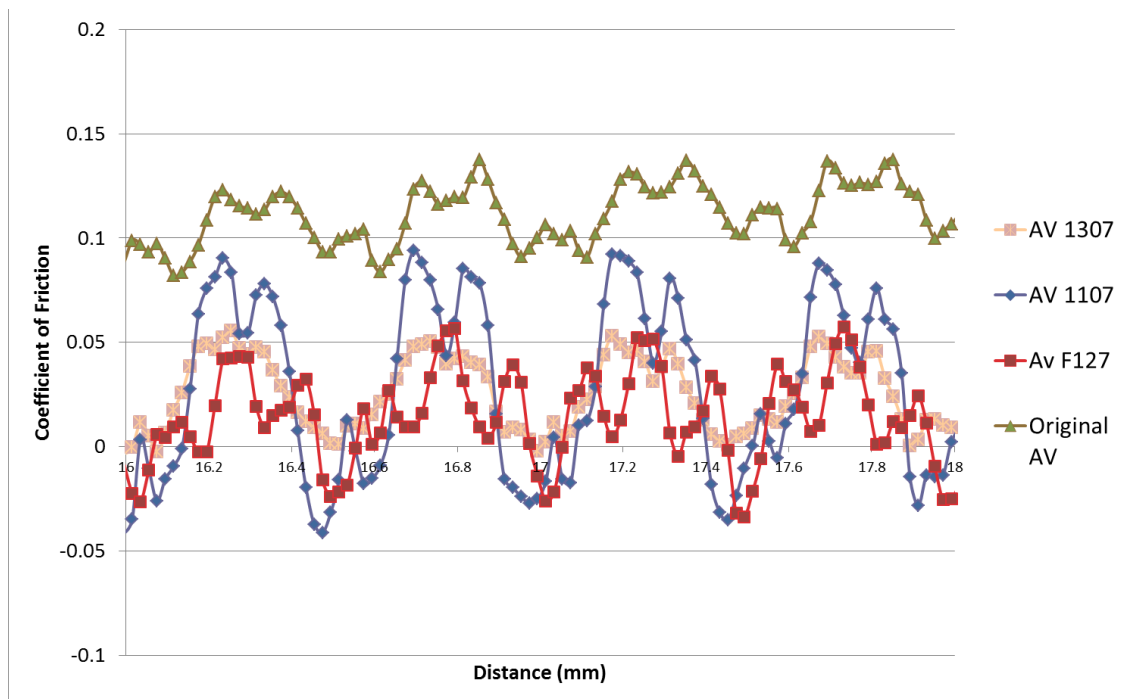


Figure 7.1.3 Coefficient traces for untreated and surfactant treated Clariti® monthly lenses

Not only does the observed COF change when the lenses are treated with a surfactant, additionally the stick-slip pattern is clearly affected. The surfactants shown here have slightly different friction traces, but the overall friction coefficients are very similar. The molecular weights of the surfactants are also very similar and significant differences would not be expected. Nonetheless, peak “stick” values decrease in the sequence: untreated > 904 > 1107 > 127 = 1307 > 1304. This suggests that the higher molecular weight and more hydrophobic surfactants adsorb more effectively at the lens surface and that it is surface adsorption that reduces friction. This will be resolved in subsequent persistence experiments.

7.2. Persistence Model C-Nano scratch tester (CSM Instruments, Peseux, Switzerland)

The standard friction program detailed in the methodology (Chapter 2) for the Nano-scratch tester (CSM Instruments, Peseux, Switzerland) consists of a 10 pass run at the

speed of 30 (mm/min) with a force of 30 (mN) and takes approximately 15-20 minutes. To measure persistence of surfactants over time, the number of passes is increased. The persistence program has 100 passes and runs for approximately 2.5 hours. (The times are approximate as they change for each run; the Nano-scratch tester (CSM Instruments, Peseux ,Switzerland) is very sensitive and reacts to any external disturbance.) 100 μ l of HPLC water is used as the lubricant and silicone coated paper as the substrate for all experiments shown here. Initially the program was left to run with no interference. This was done to ensure the contact lenses would stay attached to the mould throughout the experiment, and remain whole until the end of the experiment.

The results here are presented for the method as finally developed. Through the course of development several observations and minor difficulties were encountered. These included;

- Lenses becoming displaced from the mould and incorrect frictional data recorded (this occurred at pass 23 for a series of experiments)
- The tearing of lenses that had become very dehydrated at the edges

Figure 7.2.1 shows images of the lens, lubricant and substrate set up on the Nano-scratch tester (CSM Instruments, Peseux ,Switzerland), before and after the 100 pass experiments.

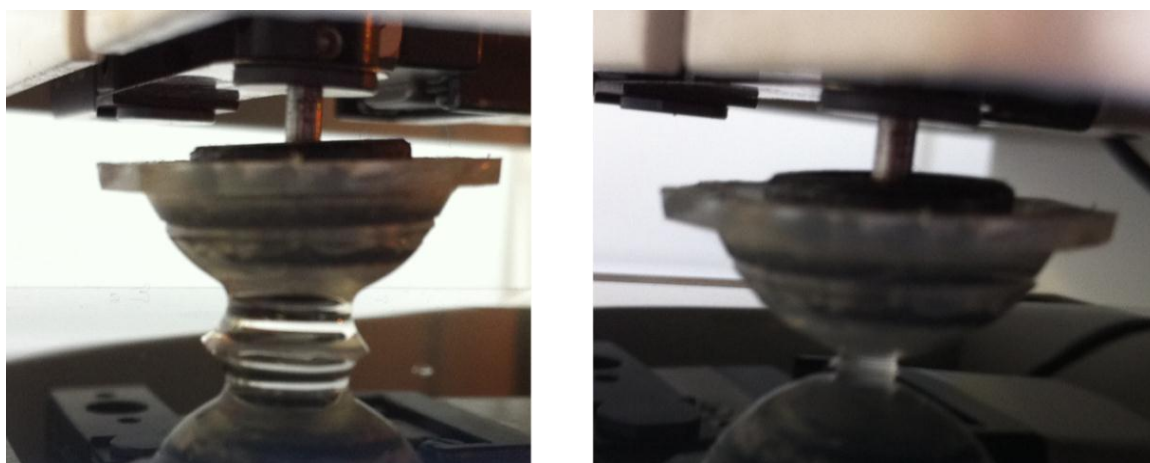


Figure 7.2.1 Photographs of friction set up. Pre (left hand photograph) and post (right hand photograph) 100 pass experiment with no elution.

Two approaches were adopted: one where the lubricating liquid was left unaltered, which had some disadvantages and as a consequence a modified model was created in which the lubricated liquid was removed and replaced. This was implemented in order to measure the surface tension of the eluted liquid as was done in both of the previous elution models A and B.

The volume of lubricant present at the start of all experiments is 100 μ l; this volume is shown in the left hand image. The right hand image shows the lubricant volume at the end of the experiment, it is clear that there is considerable reduction in volume over the 2.5 hours. However there is still lubricant present throughout the whole experiment.

It has been noted in earlier sections of this thesis (Chapters 3 and 5) that Clariti® lenses show greater lens-to-lens and batch-to-batch variability than other lenses. This has been associated with the elution of polyvinyl pyrrolidone (PVP), which is generated in the lens fabrication process (as distinct from pre formed PVP being incorporated into the lens matrix). This results in contact lenses with different elution histories. The very sensitive friction methodology has demonstrated these differences quite clearly and examples are shown in Figure 7.3.1 of four different lenses. This makes the point that reproducible types of behaviour are observed.

7.3.Results

COF is a function of the substrate, lens and lubricant. In this case a relatively hydrophobic substrate is used because it expands the differences between test materials (eg different contact lenses). Whereas two low friction materials would show very similar traces on a Melinex® (more polar) substrate, significantly different values are found using silicone coated paper. Because COF is dependent on the characteristics of the lubricant and lens, it is at first sight, difficult to predict in a closed system (fixed lubricant volume). Surfactant elution from the surface of the lens will cause an increase or decrease in COF. This problem is compounded with clarity lenses because of the inherent variability in the quantity of elutable PVP remaining in the lens at the times of test. In consequence, initial experiments were carried out in a closed system and these were followed by experiments where the lubricant (HPLC water) was

changed at intervals. This was to isolate effects of changes in the lens surface from those involving modification of the lubricant through surfactant elution from the lens surface.

The friction trace for each Clariti® lens is presented on separate axes. An averaged data plot is not used (initially) because Clariti® lenses have shown to be variable throughout the results presented in this thesis. Figure 7.3.1 and Figure 7.3.2 refer to results from the no elution friction methodology and Figure 7.3.3 -Figure 7.3.7 refers to results from the elution friction methodology.

Figure 7.3.1 shows the friction traces for untreated Clariti® monthly lenses over 100 passes.

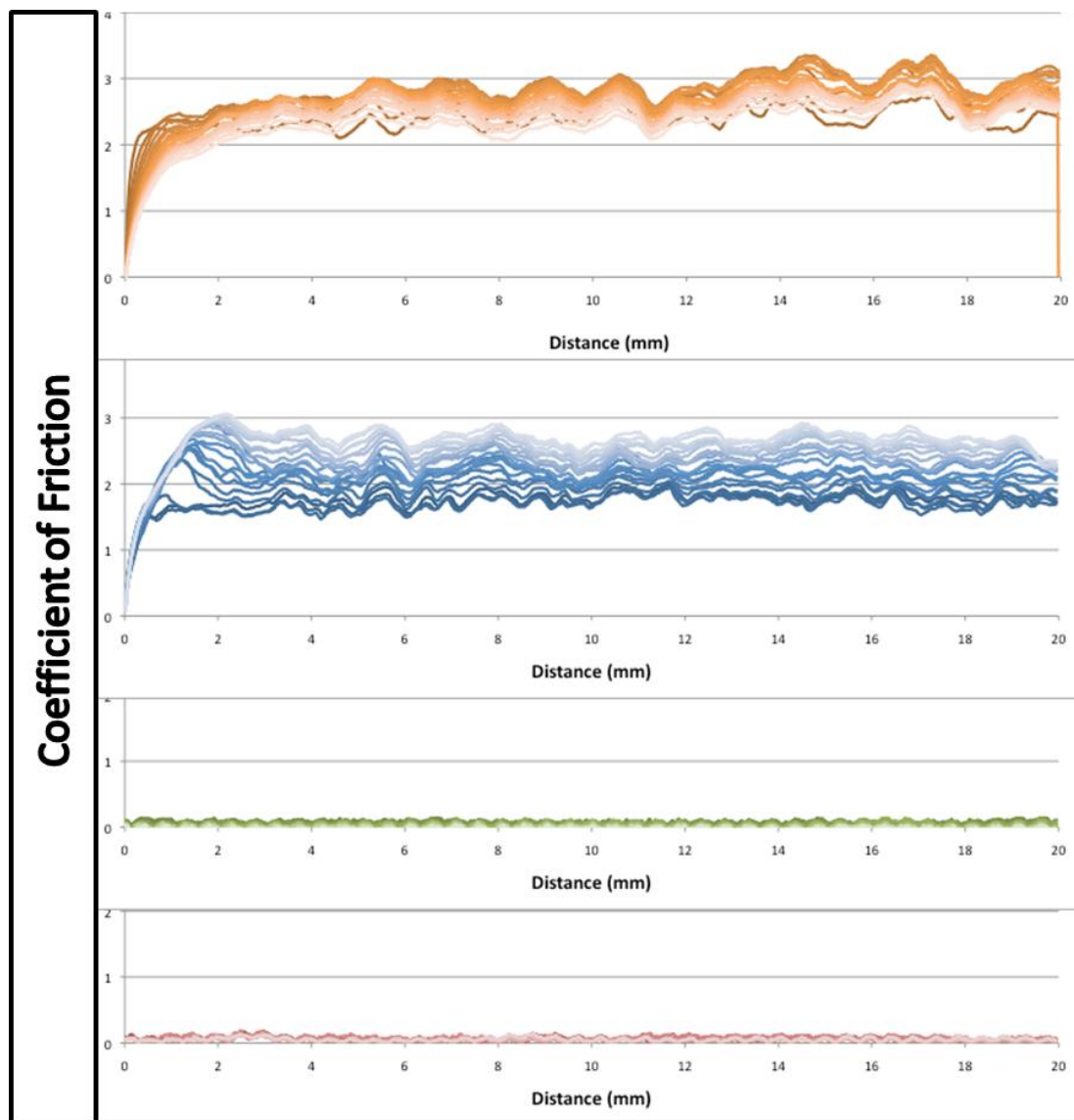


Figure 7.3.1 100 pass friction persistence model program. Untreated Clariti® monthly lenses with HPLC water lubricant and silicon coated paper substrate with no elution.

There are a total of four experimental runs presented on the graph. The darker lines on the graph are the passes earlier on in the 100-pass run. Runs 1 and 2 (orange and blue) are very similar and have several overlapping passes. The friction traces range from 1.5-3.5(units) and there are progressive changes throughout the experiments. The friction traces in run 1 tend to increase over time and the traces in run 2 reduce over time. Runs 3 and 4 (green and pink) are very similar to each other, but show much lower frictional forces than the first two runs. The lenses in runs 3 and 4 seem to be more lubricated than those in runs 1 and 2, from the start of the experiment and continue to show low friction traces up until the end of the experiment. Previous results for Clariti® lenses, presented in the thesis, have shown Clariti® to be a variable lens (even within the same batch). Clariti® packing solution does contain Pluronic® F127 and an increased amount may be present in the lenses used for runs 3 and 4. This range of behaviour can be explained by varying amounts of surfactant present at the contact lens surface.

Figure 7.3.2 shows the friction persistence model results for Clariti® monthly lenses that have been treated with a F127 1% solution.

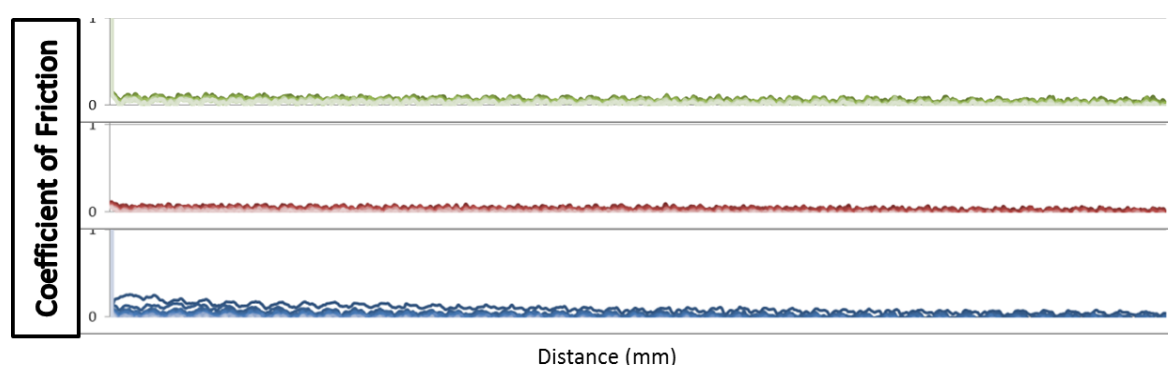


Figure 7.3.2 100 pass friction persistence model program. F127 treated Clariti® monthly lenses with HPLC water lubricant and silicone coated paper substrate with no elution.

The friction traces are low and similar to runs 3 and 4 from Figure 7.3.1. This would indicate that the lenses in runs in 3 and 4 do still have surfactant present at the surface, which is persistent after a brief wash in HPLC water.

The Nano-scratch tester (CSM Instruments, Peseux ,Switzerland) is an instrument that produces load and movement conditions broadly similar to those in the eye. It is clear from Figure 7.2.1 that the lubricant is evaporating over time. This volume reduction does not necessarily cause an effect in all cases (the technique will operate with as little as 5 μ l). The observed variations could be due to differences in residual surfactant, but in the case of Clariti[®], lens-to-lens variation (residual eluant) is known to be a considerable issue. The friction over time and number of passes does not change a great deal because the surfactant molecules are contained within a closed system. The natural system of the eye is not closed, there is tear turnover and it is important to incorporate this into the in vitro model through continuous elution.

Elution Friction Methodology

When a contact lens is placed in the eye it is continuously washed with tears. As the friction method developed, an elution step was added to simulate the effect of tear drainage. As the experiment proceeds 100 μ l of HPLC water is removed and replaced simultaneously, every 10 minutes. The use of this technique is illustrated in Figure 7.3.3 which shows friction traces over 100 passes of an untreated Clariti[®] lens that involved multiple elutions. The effect of progressive elution can be clearly seen. Figure 7.3.3 together with Figure 7.3.6 and

Figure 7.3.7, illustrates the value of this low volume friction model.

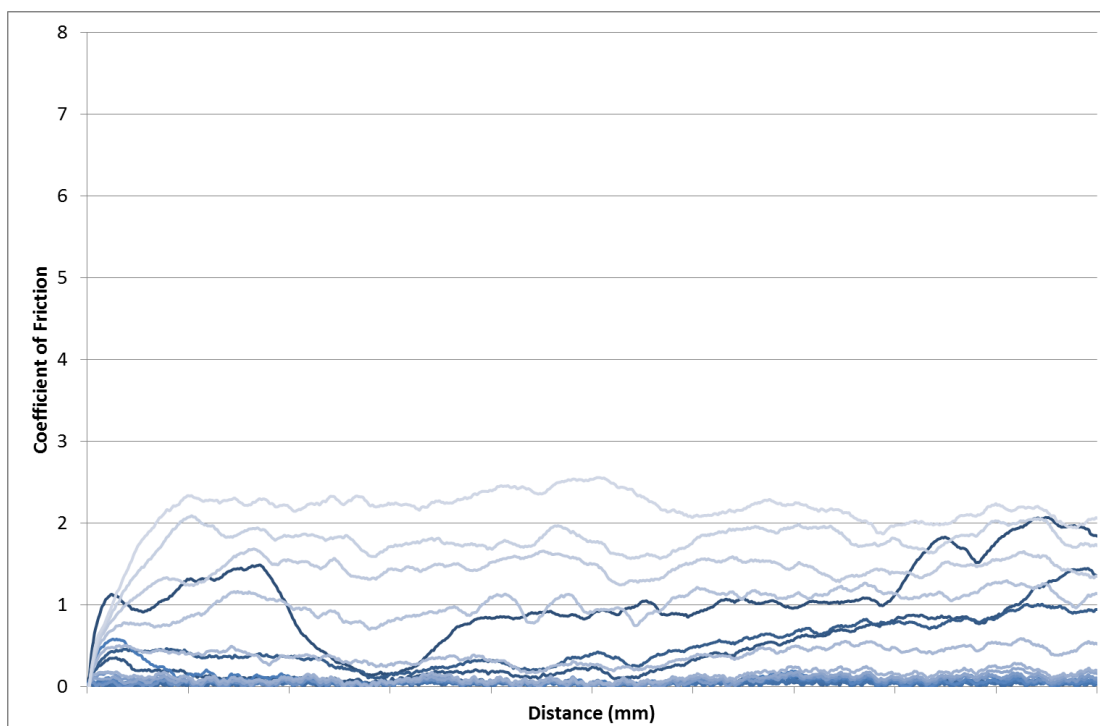


Figure 7.3.3 Untreated Clariti® Monthly lenses 100 pass Friction persistence model program. HPLC water lubricant and silicone coated paper substrate. Elution at 10 minute intervals.

The traces are darkest at the start of the run and get lighter for each subsequent trace. The graph shows the first pass as the most variable (similar to those shown in Figure 7.3.2). The frictional forces then decrease and stay close to 0.1 (units) until pass 75, where the friction traces start to rise and rapidly increase every 5 traces onwards. This graph presents the friction traces for just one lens.

The changes shown from pass to pass in Figure 7.3.3 show that the removal and replacement of HPLC water removes surfactant present at the surface of the lens and in turn displays increased coefficient of friction and stick slip values.

Figure 7.3.4 and Figure 7.3.5 shows three additional elution model traces for untreated Clariti® lenses.

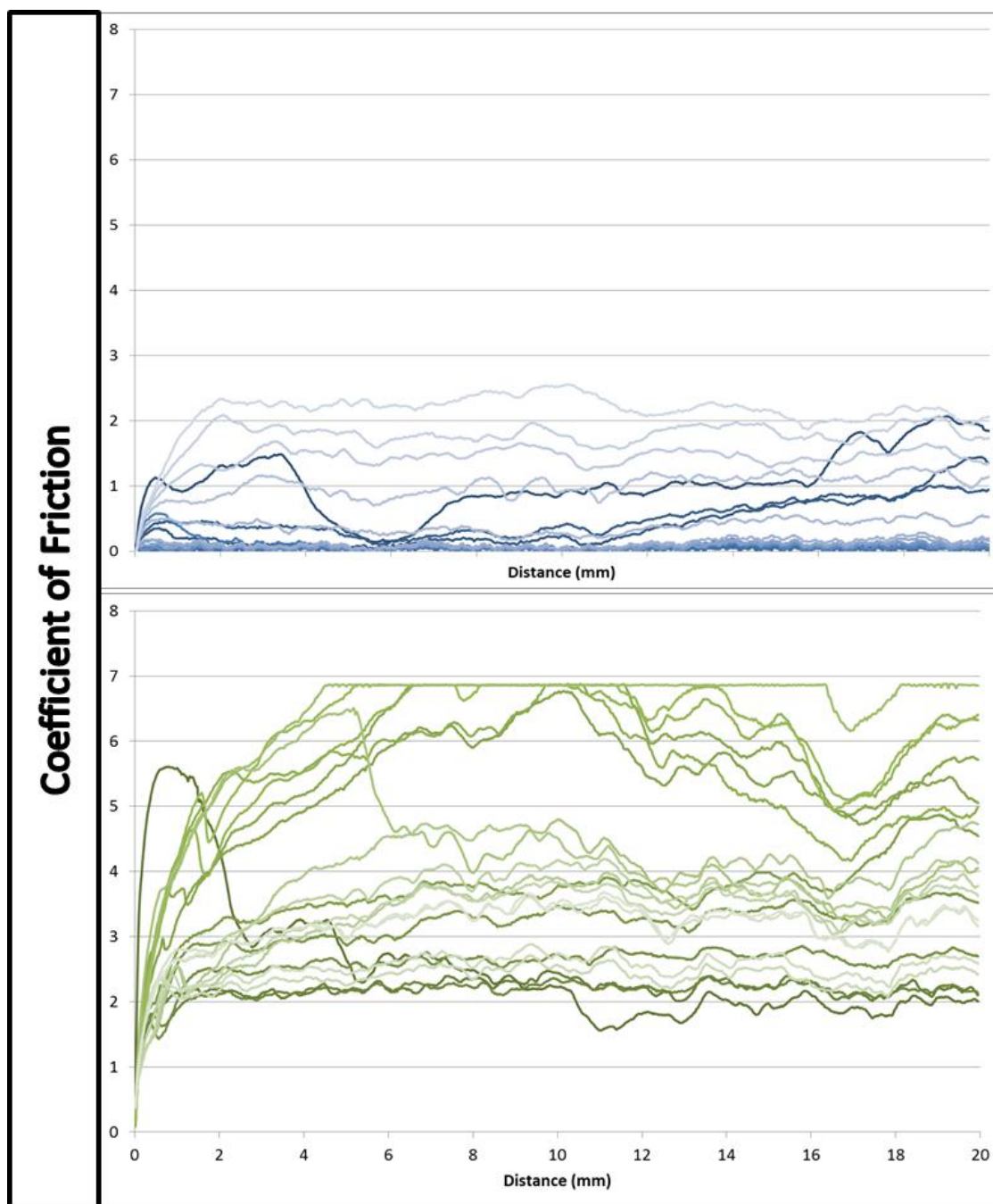


Figure 7.3.4 Untreated Clariti® Monthly lenses 100 pass Friction persistence model program. HPLC water lubricant and silicone coated paper substrate. Elution at 10 minute intervals runs 1 and 2

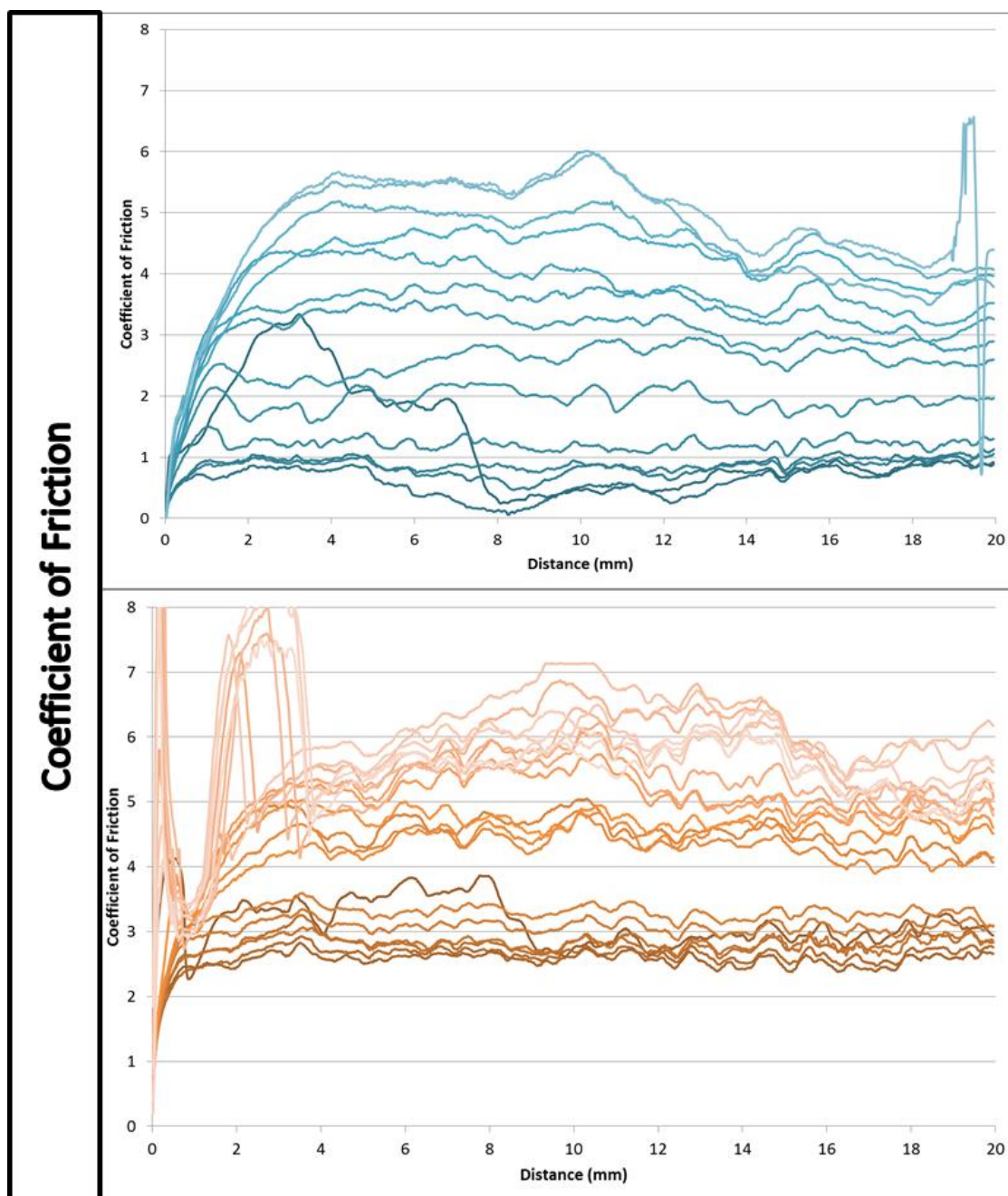


Figure 7.3.5 Untreated Clariti® Monthly lenses 100 pass Friction persistence model program. HPLC water lubricant and silicone coated paper substrate. Elution at 10 minute intervals runs 3 and 4

Each run is presented in a different colour and the darkest lines are the early passes in each experiment and they get lighter for each subsequent pass. The coefficient of friction values are much higher than those previously presented in the chapter. In run 2 there seems to be an enforced plateau at a COF of 7, this is because of instrumental limits at the settings used. In general the runs show a progressive friction increase with every subsequent pass. This indicates that the lubricity of the lens surface changes as

the HPLC water is removed and replaced. This could be because of surfactant (F127 from packing solution) removal and possibly lens dehydration. There is also variability between the lenses. Interestingly, the early traces for all four runs show similar behaviour to the four traces in Figure 7.3.1 for the no elution experiments.

Figure 7.3.6 shows the friction traces for 1 Clariti® monthly lens, that has been treated with a F127 1% solution.

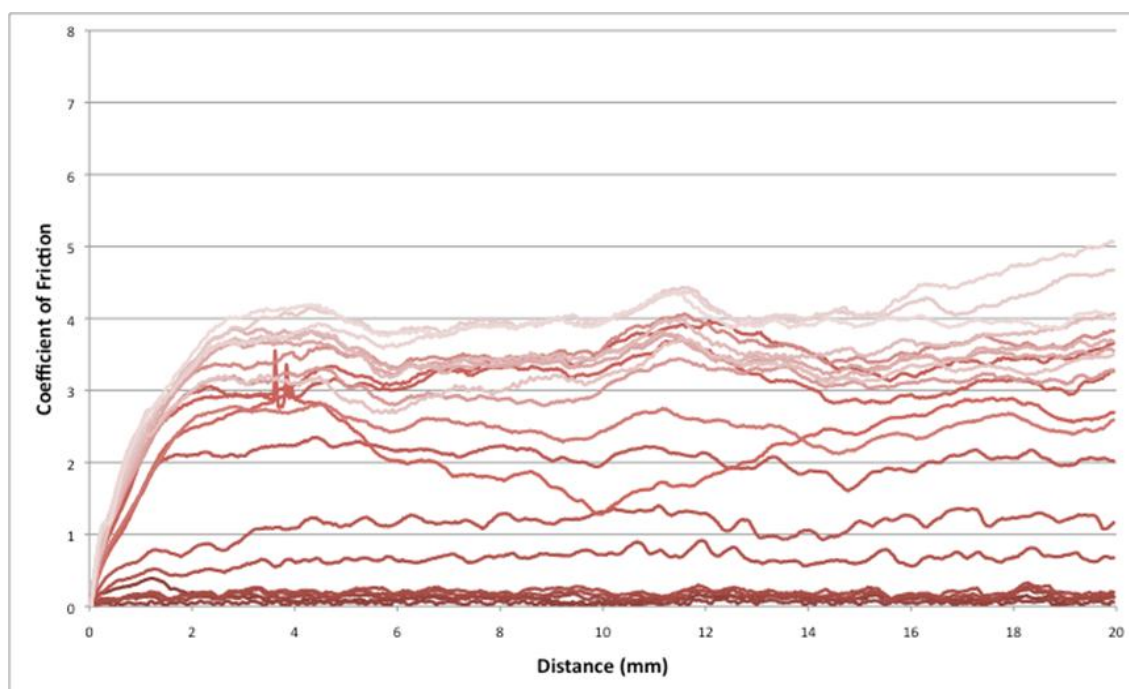


Figure 7.3.6 F127 treated Clariti® Monthly lenses 100 pass Friction persistence model program. HPLC water lubricant and silicone coated paper substrate. Elution at 10 minute intervals.

The traces are darkest at the start of the run and get lighter for each subsequent trace. The first trace sits at about 3 (units) and then the friction traces reduce as expected. It is difficult to see on this graph at exactly which pass the traces start to increase, but they do continue to increase rapidly up until the 100th pass. Figure 7.3.2 and Figure 7.3.3 show that the friction traces increase when the water is continuously replaced. There is very little difference between the frictional behaviour of pre-treated and untreated Clariti® lenses. The water is removing the surfactant from the surface of the contact lenses.

Figure 7.3.7 shows the friction traces for three F127 treated Clariti® monthly lenses.

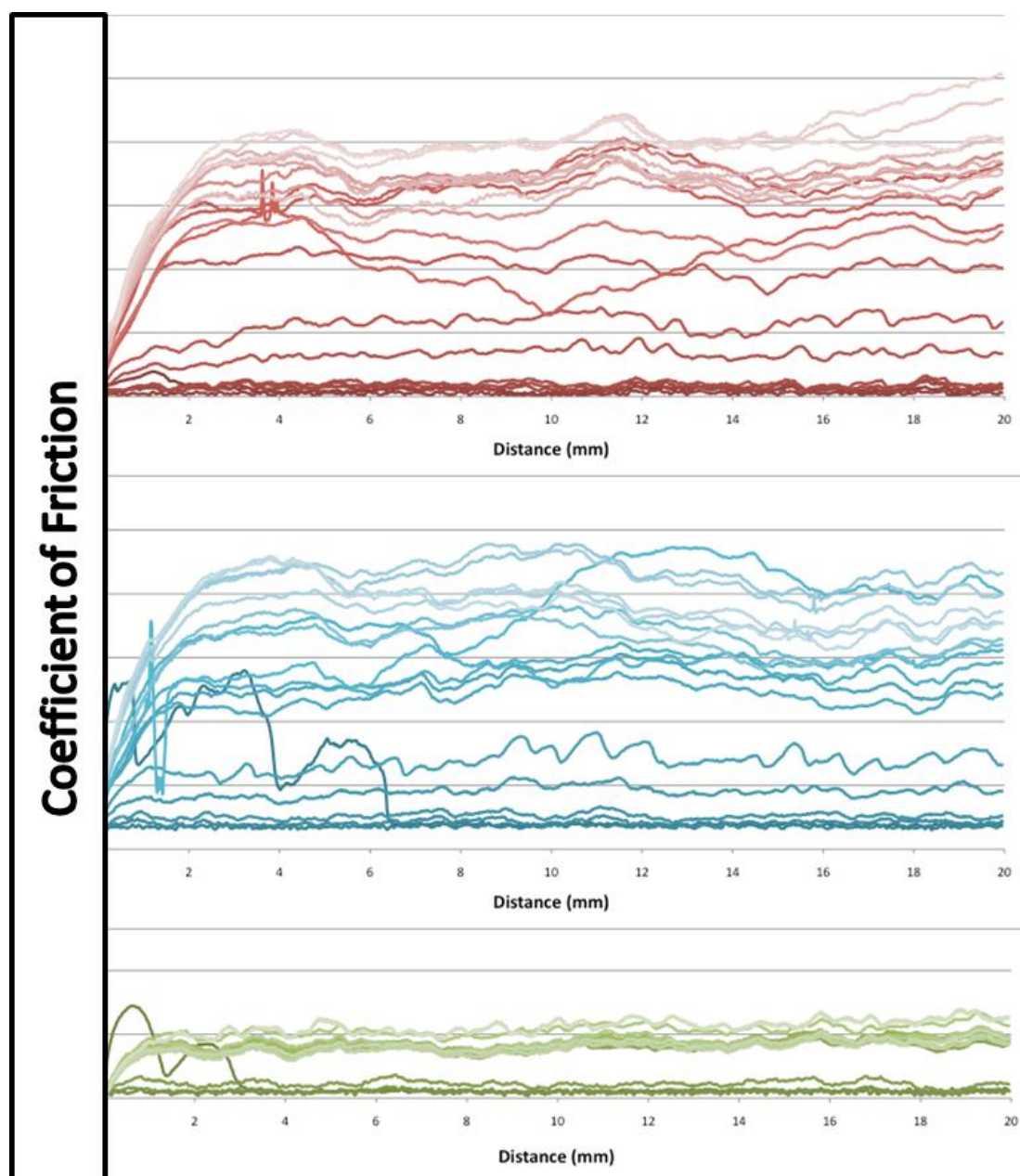


Figure 7.3.7 F127 treated Clariti® Monthly lenses 100 pass Friction persistence model program. HPLC water lubricant and silicone coated paper substrate. Elution at 10 minute intervals all runs

Each run is presented in a different colour and the darkest lines are the early passes in each experiment and they get lighter for each subsequent pass. Runs 1 and 2 (red and blue) have very similar traces for all 100 passes. Their highest friction values fall between 4 and 5 (units). The third run (green) starts out very similar and the friction traces do increase towards the end of the run, however the highest friction values are around 1 (units). Throughout the work presented in this thesis, Clariti® and Clariti® 1 Day have shown to have variable unstable surfaces. The difference between experimental runs could be caused by increased surfactant persistence. This may be because of increased amounts of residual PVP present in the lens material.

The combined complexity of the variable Clariti® lens surfaces, the fact the PVP of a wide range of molecular weights is being eluted, and the presence of F127 (which is known to interact with PVP) provide an accumulation of variability. None the less, this does indicate the potential that Clariti® has for improvement and enhancement using the unusual nature of its surface.

Graphical representation of elution-related changes

The methodology shows different frictional behaviour between eluted and no elution experiments and treated and untreated lenses. Figure 7.3.8, Figure 7.3.9 and Figure 7.3.10 show the COF values at 10mm for each pass. This will make the progressive COF changes much easier to compare and understand in a quantitative way. The frictional properties change as a function of number of elutions and number of passes.

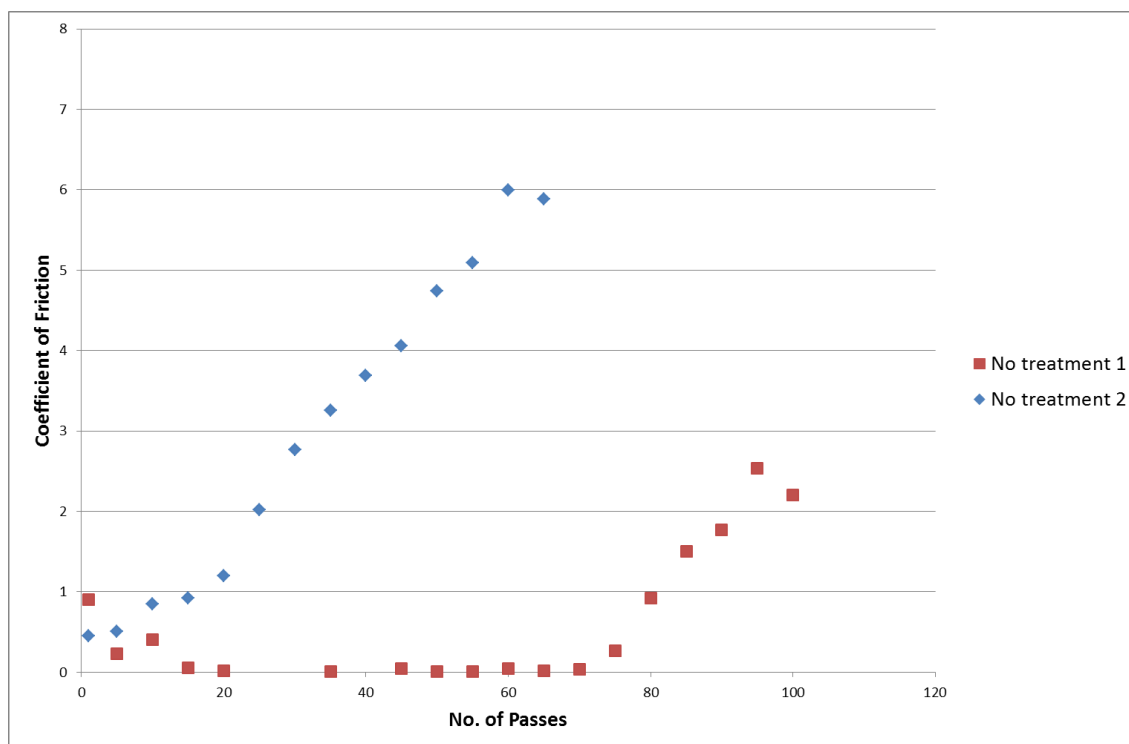


Figure 7.3.8 Coefficient of friction value of untreated Clariti® lenses at 10mm for each consecutive pass for the 100 pass persistence elution experiment.

The first elution experiment of the untreated Clariti® lenses in Figure 7.3.8 shows significantly different behaviour between the two lenses. The COF progression for lens 1 is steady, and only starts to increase at pass 75. In contrast the COF progression for lens 2 starts to increase almost immediately and continues to rise.

Figure 7.3.9 shows a similar graph for F127 treated Clariti® lenses.

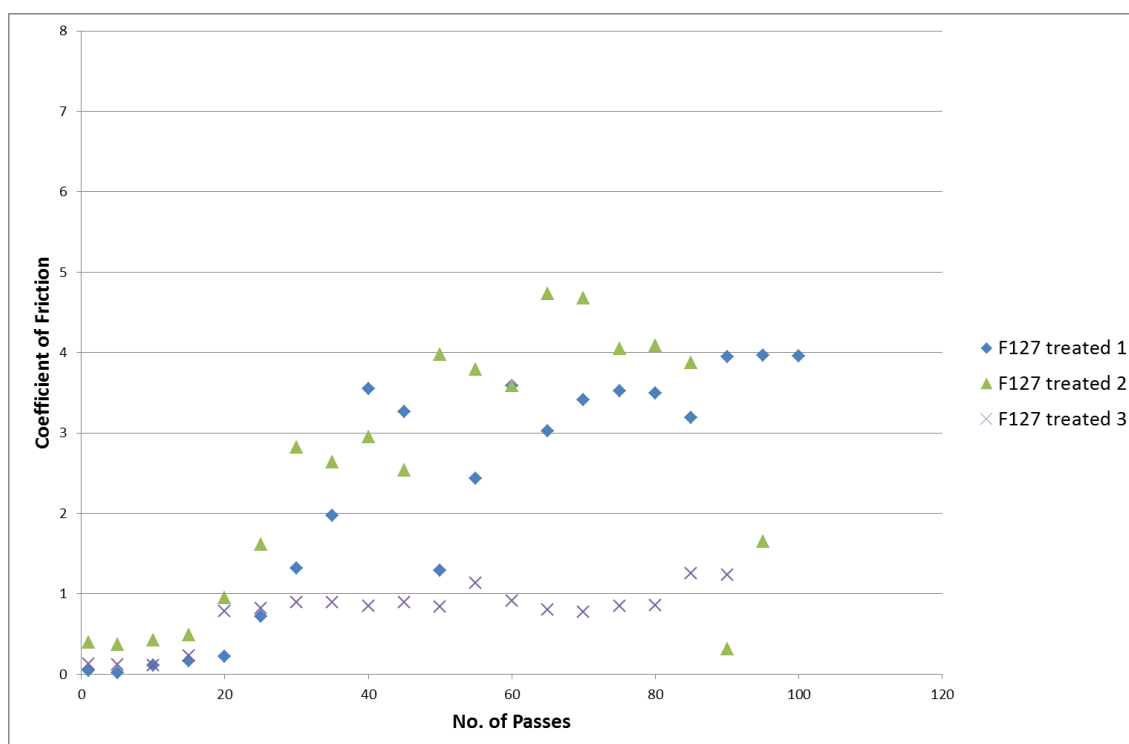


Figure 7.3.9 Coefficient of friction value of F127 treated Clariti® lenses at 10mm for each consecutive pass for the 100 pass persistence elution experiment.

The data shown in Figure 7.3.9 has a much gentler COF incline; the COF however, starts to increase at pass 20 similar to the data from the untreated lenses. Runs 1 and 2 shows very similar data values and similar shaped graphs, run 3 has much lower steady COF values throughout the experiment.

The data presented in Figure 7.3.8 shows a sharp incline in COF for one lens. This indicates that any lubricious surface behaviour soon reduces through washing and agitation of the lens. In contrast Figure 7.3.9 shows the COF value to stay relatively low until pass 20; this is where the COF value starts to rise for each run.

The data from treated and untreated materials present lenses that behave differently to each other. This difference can be attributed in both cases to the variability of Clariti® and variable amounts of residual PVP present in the Clariti® materials.

The average COF values for the treated and untreated Clariti® lenses are presented in Figure 7.3.10.

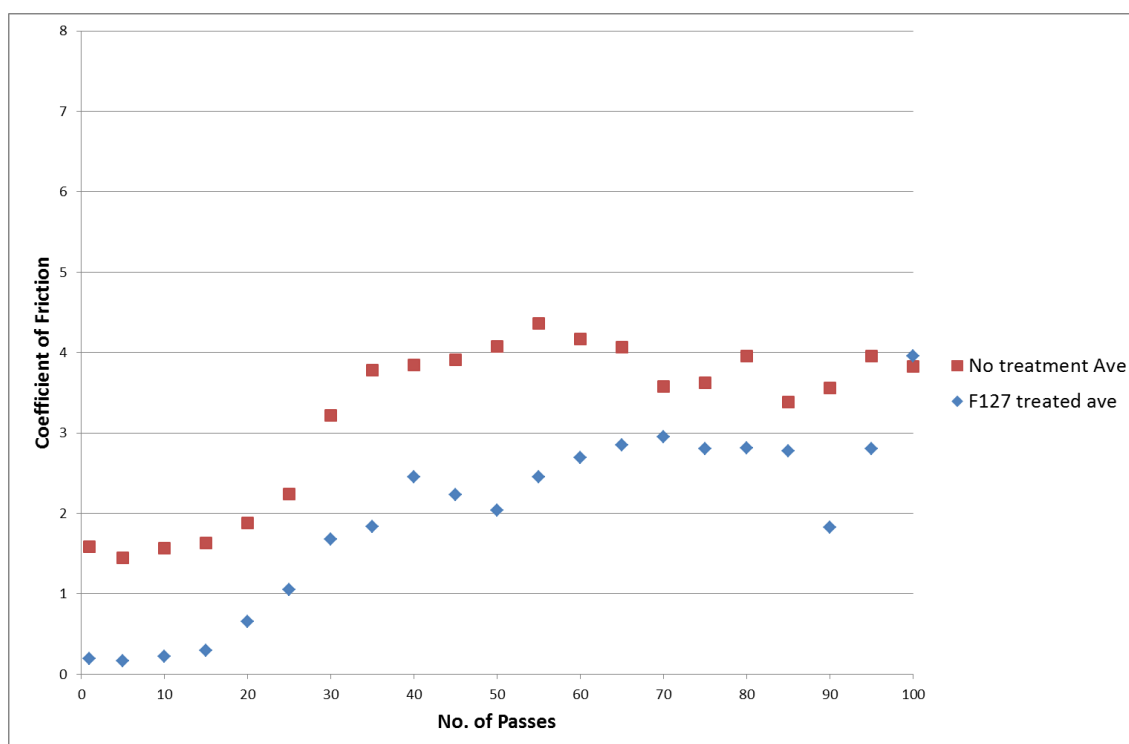


Figure 7.3.10 Average Coefficient of friction values for treated and untreated Clariti® lenses at 10mm for each consecutive pass for the 100 pass persistence elution experiment.

There are clear differences between the data for treated and untreated lenses. Although the shapes of the graphs are similar, the initial COF is 1 unit lower for the treated lenses. This indicates that the initial insertion lubrication of the treated lenses is greater than that of the untreated lenses. This in turn results in increased lubrication throughout the experiment.

These results complement those presented in earlier chapters in reference to the surfactant treatment of Clariti® lenses. The surface behaviour of Clariti® lenses is modified and improved (in regards to wettability and COF) when treated with surfactants, in particular Pluronic® and Tetronics®. The surface modification (under the friction model experimental conditions) is observed up until the completion of the run (approximately 2.5 hours – 3 hours).

7.4. Discussion and Conclusion

The aim of this chapter is to demonstrate the validity and potential of a third in vitro model, which will enable differences between surfactant molecular weight and hydrophobicity to be investigated with the use of small liquid volumes. The

methodology confirms again that the high molecular weight hydrophobic surfactants such as Tetronic®1304 appear to have greater influence and persistence (see Figure 7.1.2).

A common draw back from elution models A and B is the volume used. The volume of tears in the eye is much lower than the volumes in both of these models. The Nano-scratch tester (CSM Instruments, Peseux ,Switzerland) however allows for volumes as low as 20µl to be used.

To measure surfactant persistence on a lens surface the numbers of passes were increased from ten to one hundred, this increased the experimental time from approximately 15-20 minutes to 2.5-3 hours. Over this time the lenses are subject to increased dehydration and this was observed in runs 1 and 2 of Figure 7.3.1 (no elution, no treatment). This level of dehydration was not observed in the F127 treated Clariti® lenses (Figure 7.3.2), the COF values do not change through the whole experiment. Clearly, the added F127 is retaining moisture at the surface more effectively.

In the eye the tears evaporate and drain out of the eye and are replaced continuously. Along with eyelid agitation, these mechanisms will remove surfactants from the surface of the contact lens and out of the eye. The elution friction model takes tear turn over into account.

The surfactant molecules will be in one of three places (see Figure 7.4.1); the surface of the lens, the surface of the substrate or in the lubricant solution. It is important to remember that excess surfactant solution was washed from the lens before the experiment commenced. This means that the only surfactant introduced was adsorbed at the surface of the lens. Surfactants adsorb preferentially at surfaces and it is unlikely that an appreciable quantity would be in solution. It is possible that some molecules may be absorbed to the substrate, but because they have to pass through the lubricant solution; it would be unlikely to be many molecules at this position. Most molecules would remain at the surface of the contact lens and this presence and modification is the dominant effect in reducing the COF. In addition to this, there is no evidence that reducing the surface tension of the liquid by a small amount is the

dominant effect in comparison with desorption and that is confirmed by the fact that there is only a small concentration of surfactant present and the elution of lubrication solution does not cause immediate effect to the COF data. It is the gradual elution of surfactant from the surface that causes the COF to increase.

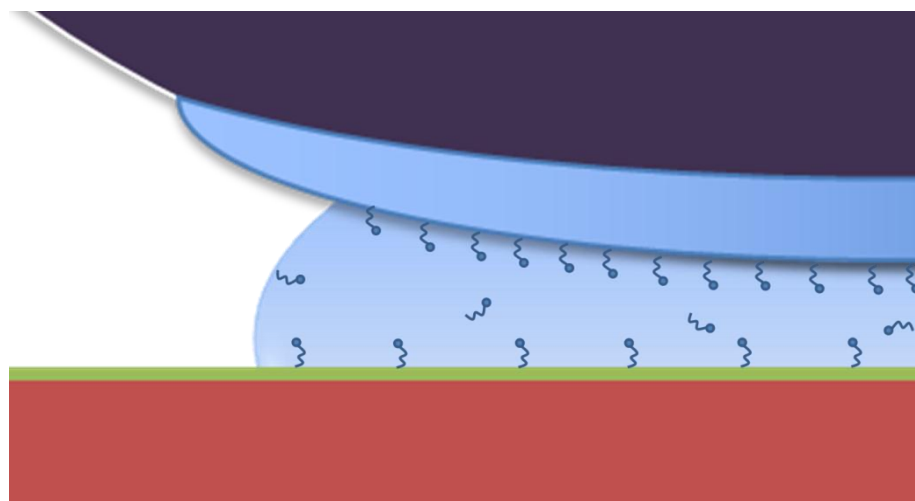


Figure 7.4.1 Schematic of surfactant molecules adsorbed to the contact lens surface, in solution and adsorbed to the substrate.

This does not mean to say that MPSs would not have a specific effect on friction due to changes in the lubricity of the liquid; it is simply that in a MPS there is a significant concentration of surfactant. In the eluted liquid in these experiments the surfactant concentration is very low.

The data from the elution friction model shows the COF rising over time for all runs, the initial COF is always much lower than the final COF. It is also possible to see differences between the surfactant treated and untreated Clariti® lenses. The treated lenses show a lower COF for a greater number of passes and a lower average COF. As with all of the data presented for the Clariti® materials, there is lens-to-lens variation. From the data presented in this chapter, the Clariti® lenses that behaved usually, displayed lower COF than the other lenses. This could indicate higher levels of PVP present at the lens surface and greater surfactant/PVP interaction.

A frequently reoccurring point throughout this thesis is the unusual behaviour of Clariti® materials. The surface of Clariti® is unstable, deteriorating continuously and eluting PVP. In addition to this its packing solution has considerably more surfactant

(Pluronic® F127) than any other packing solution. This means that the lens is soaked in F127 solution from the production process until experimentation; this will most likely be a matter of months. In this time the surfactant will interact with the PVP present at the lens surface (which will be increasing over time). The baseline data acquired from Clariti® lenses are unlikely to show consistency when there is substantial surfactant/lens interaction taking place prior to any experimental treatment.

There are two complementary measurement techniques presented in this thesis; models A and B measure the surfactant in the eluting solution, whereas this method measures the effect of residual surfactant at the lens surface.

The friction persistence model is a useful tool in the observation of surfactant persistence at the surface of a contact lens. It is possible to see surface differences between the F127 treated Clariti® and untreated Clariti® lenses. The model can detect surface modification achieved through surfactant treatment, and changes over time. The silicone coated paper substrate allows for greater distinctions between samples and between individual passes to be seen.

Only one surfactant/material combination is used in these experiments, however the Nano-scratch tester (CSM Instruments, Peseux ,Switzerland) has shown differences between surfactants (see Figure 7.1.2 and Figure 7.1.3) and materials (see section 3.4) for other experiments. Surfactant differences would also be observed for the friction persistence model as were observed from both elution models. This method was carried out at the very end of the experimental work and would obviously have been extended to other material/surfactant combinations if time had allowed.

Key points:

- The friction persistence models are useful tools, particularly the elution variant. In contrast to the elution models A and B, which measure eluted surfactant, the friction model measures the effect of surfactant remaining at the surface.

- The molecular weight and hydrophobicity of poloxamer/ poloxamine surfactants are both influential in controlling adsorption and persistence.
- It is clear the Clariti® lenses, as observed in this chapter (confirming what has been found in previous chapters) have very mobile surfaces and the elution of PVP (probably containing fragments of siloxy monomer), means that the history (time, agitation and storage conditions) of the lens will alter the nature of the lens surface.

Chapter Eight

Concluding Discussion and
Suggestions for Further
work

8. Concluding Discussion and Suggestions for Further work

The overriding aim of the work described in this thesis was to investigate the interaction between hydrogel and silicone hydrogel contact lens materials and multi-purpose care solutions; in particular the persistence of surface-active ingredients contained in multi-purpose solutions on different contact lens materials. It has been suggested earlier on in the thesis that certain lens materials could be paired with certain surfactants. To understand the interactions it is important to understand and characterise the materials and solutions separately.

In a completely novel approach to surface characterisation, the dehydrated surfaces of contact lenses were investigated through the use of the sessile drop technique and through the use of polar and non-polar probe solutions; the surface energy of each material was calculated. This gave an indication of the molecular behaviour at the surface. There were distinctions between the types of contact lens materials. Conventional hydrogels behave differently to silicone hydrogels, for some examples this can be attributed to different water contents. However plasma coated silicone hydrogel materials showed very similar surface energy behaviour to conventional hydrogel materials. The coating present effectively masks the normal hydrophobic behaviour of the silicone. This work examined if it possible to modify and mask hydrophobic surface behaviour through surfactant treatment.

Many contact lenses are currently modified to improve surface wettability; this is often done through addition of surfactants or wetting agents. Surfactants have hydrophobic and hydrophilic 'poles' this means they are attracted to surfaces. The hydrophobic parts of a surfactant molecule are attracted to the hydrophobic domains on a contact lens surface. This effectively creates a new hydrophilic surface on the contact lens and will increase the wettability. This modification is not permanent like the plasma coating, and is removed through either washing or wear. Air Optix® Aqua is an example of a where a wetting agent is added and after one wash it is removed.

Plurionics® and Tetronics® were selected as the basis of this study of contact lens modification as these surfactants are often used in contact lens care solutions. It is important that surfactants used in the eye cause no adverse effects or discomfort. Large molecular weight surfactants such as the Plurionics® and Tetronics® are used as they are unable to penetrate the corneal cell walls and are non-toxic to the ocular environment.

These triblock copolymers can differ in both molecular weight and hydrophobicity. It is possible to see behavioural differences between these polymers through surface tension measurements. Both static and dynamic surface tension measurements were used to characterise all the surfactants here. The dynamic surface tension data are especially interesting, they give an indication of how a surface will behave under dynamic conditions such as cleaning and in the eye.

It is known that surfactants can modify the properties of a contact lens surface; however this modification is not permanent and is removed during lens wear. Many tear components have similar surface tension behaviour to the surfactants used to modify lenses; this causes difficulty when measuring in vivo persistence. It is therefore important to create an in vitro eye model to measure the surfactant persistence.

Lenses such as Clariti® and Clariti® 1 Day became of great interest as they were shown to have the most variable surface behaviour. They also show a large polar fraction of surface energy, this would indicate increased wettability and possibly comfort. This was hypothesised to be due to PVP leaching from the matrix of the lens.

As this work was drawing to a close a visiting Erasmus student was able to obtain some results that aid the explanations and interpretations from this work. Some of those observations are summarised in this discussion.

Congo red dye was used to determine the presence and concentration of PVP. This is possible because the Congo red molecule binds to the PVP molecule and as a result the colour intensity of the contact lens material is affected. Using this method, the lens material was shown to leach PVP (see Figure 8.1); possibly low molecular weight PVP that may cause irritation to the eye.[151]

Figure 8.1 shows a range of commercially available contact lenses, most of which contain PVP.



Figure 8.1 Selected contact lenses coloured with Congo red dye.

There are clear differences between Medalist (38% water, no PVP) and the other lenses, which do contain PVP. It is also possible to observe a colour intensity difference between the Acuvue® lenses, Clarity® 1 Day lenses. Figure 8.2 shows the numerical data related to the image in Figure 8.1.

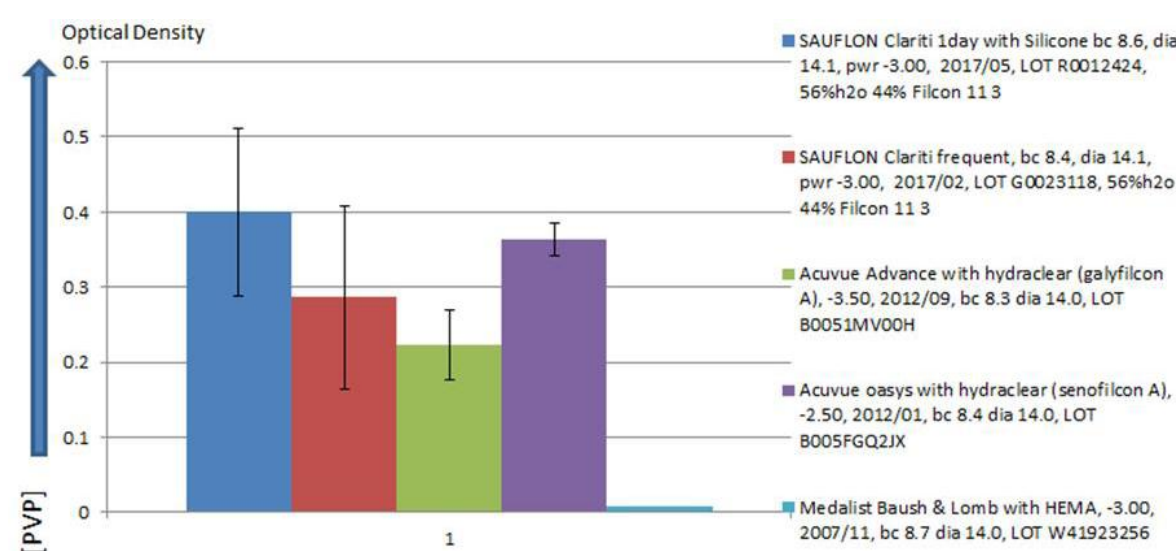


Figure 8.2 Determination of PVP concentration of several commercially available contact lenses using the colorimetric method and Congo red dye.[151]

It is clear that the amount of PVP varies from lens to lens, with Clariti® 1 Day showing the greatest amount of PVP. Another interesting point that can be taken from this data is the variability of the Clariti® results. Both Clariti® and Clariti® 1Day have similar sized error bars and these are more than double the size of the error bars for the Acuvue® materials. From the work presented in this thesis it is known that PVP elutes from the surface of the contact lens into the packing solution. Figure 8.3 shows the level of PVP present in the corresponding packing solutions.

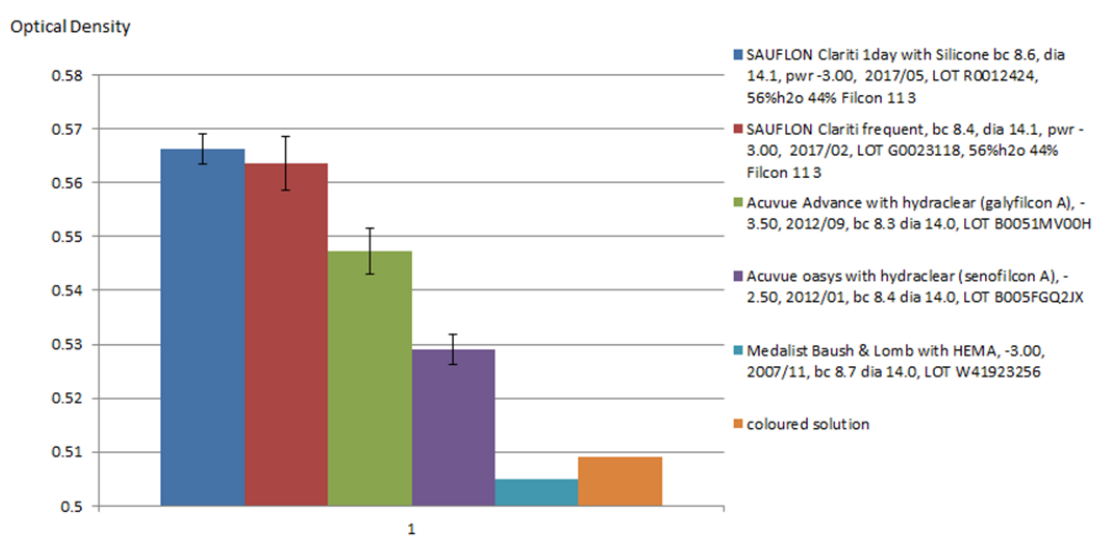


Figure 8.3 Determination of PVP concentration in the packing solution of several commercially available contact lenses using the colorimetric method and Congo red dye.[151]

The highest optical density directly correlates to the colour intensity and concentration of PVP. There are clear differences between the contact lens packing solutions. The data follows a similar order to that of Figure 8.2 with the exception of the Acuvue® lenses. Clariti® lenses contain more PVP and elute more into the packing solution.

The above data also shows Clariti® 1day to have more PVP in the packing solution and on the contact lens. This data complements the persistence differences seen in Chapter 5 where Tetronics® show greater modification and persistence on the Clariti® 1Day material in comparison to Clariti®, Acuvue® Advance® and Focus Dailies® lenses.

The Clariti® 1Day data also complements the lens differences found in section 3 and to the suggestion of altered manufacturing process and reduced extraction time.

The surfactants used in the work present in this thesis (Pluronic® and Tetronics®) are high molecular weight triblock copolymers that are often found in contact lens care solutions. These surfactants are used to perform a variety of tasks including cleaning and rewetting the contact lens surface.

The FDA requires the concentration of surfactant in an approved MPS to be at or over the critical micelle concentration. For simple surfactants this is a reasonable requirement; surfactant detergency increases up until the CMC with no change above the CMC. However for high molecular weight surfactants that are able to form monomolecular micelles, it is an unreasonable a rather illogical issue. These surfactants can surround and remove dirt and debris at concentrations below a classical CMC point. Their surface tension data does not show a clear inflection at the CMC; there is a gradual transition from very low concentrations to the nominal post-CMC surface tension value with no clear change in behaviour. The CMC and dynamic surface tension behaviour do not give an indication into the cleaning ability of a contact lens MPS. There is no simple correlation with dynamic CMC and surface tension.

The dynamic surface tension results were influenced by several properties such as molecular weight, structure and hydrophobicity. Figure 4.2.1.7 shows the dynamic surface tension plot gradient against the molecular weight of the hydrophobic component of the surfactant.

From Figure 4.2.1.7 it is clear that under dynamic conditions, surfactant molecular weight influences the ability of a molecule to reach equilibrium. This influence is greatest for hydrophilic molecules such as F127 and 1307. The hydrophobic molecules are affected by molecular weight, but the most influential property is hydrophobic drive, which allows for the molecules to reach equilibrium quickly. Hydrophobic drive can also give an indication of surfactant persistence because the air/water interface is similar to the contact lens/water interface. If a molecule has great hydrophobic drive

then it will have a greater affinity for the hydrophobic domains at the surface of a contact lens.

Turning to the question of persistence, elution model A highlights the importance of flow rate. Variation 2 (dipping) of the large scale model A has the highest flow rate and shows the shortest persistence times plus reduced distinction between the Tetronics® used. Elution model A variation 1 (combination) shows greater distinction between the surfactants and was used to assess persistence difference between dehydrated and hydrated lenses.

Clariti® 1 Day and Clariti® Monthly lenses were both dehydrated prior to surfactant treatment. The dehydrated lenses show greater surfactant persistence than those treated in the hydrated state, even after the end of the experiment. Along with surfactant release from the lens material, the contact lens surface remained modified until the end of the experiment. This increased persistence was especially noticeable for Clariti® 1Day lenses. It is known that Clariti® contact lenses are hydrated after thermal polymerisation. The wettability of the contact lens could be enhanced if the lenses were hydrated in a surfactant solution.

A similar experiment was carried out with Focus Dailies® (high polar fraction) and Acuvue® Advance® (low polar fraction) contact lenses. The small scale elution model B was used in this case. Here, there was no distinction between hydrated and dehydrated lenses or surfactants used. There was also only a small difference between the contact lens materials. This indicates that polar fraction and water content do not affect surfactant persistence.

The presence of PVP thus appears to be an important factor in surfactant persistence and when PVP is present the surfactant persistence can be increased further by dehydration prior to treatment. Clariti® contact lenses were used in most of the persistence experiments. The increased amount of PVP contained in these lenses contributed to the greater surfactant persistence in comparison to other contact lens materials. Similarly to the dynamic surface tension results; molecular weight and hydrophobicity also affects the surfactant persistence at the contact lens surface.

Focus Monthly® and Soflens 1 Day® lenses were used to study the ex vivo persistence of ReNu® MPS (which contains Tetronic® 1107). These lenses were chosen following other persistence studies in the literature and the increased surfactant persistence seen when PVP is present in a lens material. There were noticeable differences between treated and untreated lenses when assessed through elution model B (see right hand graph Figure 8.4).

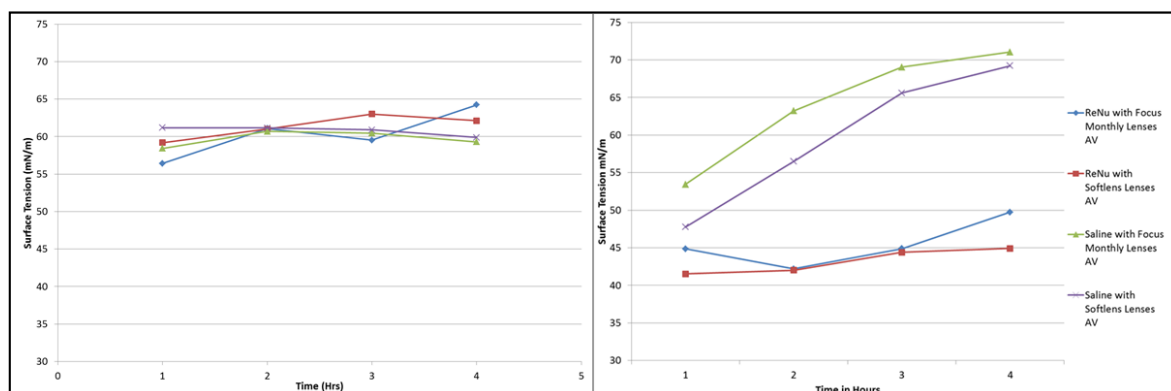


Figure 8.4 Ex vivo (left graph) and In vitro (right graph) surface tension measurements of ReNu® soaked contact lenses.

Figure 8.4 also shows that the surface tension measurements from the ex vivo experiments (left hand graph). The surface tension data are very similar regardless of contact lens or soaking solution. The ex vivo data are subject-dependent and the volume and concentration of tears is the dominating factor. For this work, ex vivo experiments are not suitable, and the small scale elution model B is still much larger than the natural eye system. The Nano-scratch tester (CSM Instruments, Peseux, Switzerland) uses very small volumes of lubricant in order to gain force/distance data. The continuous movement between the mould and substrate can simulate agitation due to eyelid movement. Standard friction methodology consists of 10 passes per measurement; to measure persistence the number of passes needed to be increased and 100 passes were chosen. HPLC water was used as the lubricant and was changed at regular intervals. The friction traces changed over time and the coefficient of friction tended to increase with time.

Clariti® lenses have shown to be variable throughout this thesis and this is reflected again in the 100 pass friction model (see Figure 7.3.1).

There are significant differences between runs 1 and 2, and 3 and 4. This could be because of the differing levels of PVP or surfactant present in the lens surface. The COF is dependent on both surface and bulk material properties; this introduces more complexity to results analysis.

The data presented in Figure 7.3.10 clearly shows that contact lens COF can be reduced by the presence of surfactants. In addition to this the surface modification and COF enhancement is persistent up until the end of the experiment, over 2.5 hours. There is only one surfactant (Pluronic® F127) used in these experiments and only one material (Clariti® monthly), hence it is not possible to compare material and surfactant differences. However the friction model methodology is highly sensitive and has shown distinctions between materials and surfactants under other experimental conditions (the standard 10 pass methodology stated in Chapter 2).

8.1. Further Work

There are many opportunities for further study following the work presented in this thesis. The friction eye model is the most 'eye-like' of all the models presented here and could be used to investigate other properties along with surfactant persistence. The most obvious extension is to apply this method to other lens/surfactant combinations. The persistence of packing solution additives used with contact lenses could also be examined by this method.

With a given surfactant-treated lens, as described in chapter 7, the eluent surface tension could be measured; this data would be directly comparable with the data produced from the previous two models A and B. The volume of eluent after every ten minute change is 100ul, this volume needs to be at least doubled if the mini du Noüy ring (KRÜSS GmbH, Hamburg, Germany) methodology was adopted. The lubricant volume could be doubled or 2 eluents could be added together.

In contrast to the above, the lubricant volume could also be reduced to reflect volumes experienced in-eye. The Nano-scratch tester (CSM Instruments, Peseux, Switzerland) allows for very low lubricant volumes to be used, these may show persistence behaviour further in line with in-eye persistence behaviour.

The friction program could be extended from 2.5hrs to 8hrs or longer to further investigate how contact lenses and surfactants behave over daily wear.

The speed and load for the friction model is set at 3030, these settings could also be altered to further mimic in-eye movement and force. The HPLC water lubricant could be replaced with tear like solution to allow for the friction data to reflect more 'eye like' behaviour.

Contact angles could be taken of the lenses pre and post runs to measure the surface energy changes of the material. Contact angles could also be taken of the lubricant on the substrate pre and post run, this would give an indication of surface tension changes or residual surfactant on the substrate.

In reference to specific materials, Clariti® and Clariti® 1Day lenses have been highlighted as unusual in each results chapter as variable. These lenses are the only

ones that incorporate VP monomers into the material mixture prior to polymerisation. The increased surfactant persistence displayed by both materials, especially Clariti® 1 Day and especially when the material is dehydrated prior to surfactant treatment, could be utilised for several applications. One of which is ocular drug delivery. The steady release of surfactant over time displayed by Clariti® 1 Day in Chapter 5 is ideal for continuous delivery of drugs to the eye. This would reduce effects of patient compliance and possible overdosing.

Appendices

9. Appendices

9.1.BCLA Posters

The Role of Surfactants in Multipurpose Solutions

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Methods-1-6

Multipurpose solutions based variously on: Pluronics 88, 87, 108 and 127, Tetricons 904, 1107 and 1304 and an ethylene oxide propylene oxide copolymer were examined. Static and dynamic techniques (together with an in vitro spillover/cleaning model) were used to obtain surface tension plus CMC data and assess cleaning. Complementary techniques (not presented here) provide data on relative surfactant persistence and tear film disruption behaviour.

Results

The first question is fundamental to the generally perceived role of the surfactant and has become more important since the advent of silicone hydrogels – does the cleaning capability as reflected in lipid removal vary with different MPS. Figure 1 provides relevant information showing (a) that the commercial MPS studied vary in lipid removal capability, (b) that total lipid cleaning efficiency lies between 80% and 95% and in no case is all the sorbed lipid removed, but (c) all MPS are much more effective than saline. It is also important to note that cleaning efficiency shows material dependence and also decreases with duration of wear and progressive diffusion of lipids into the lens matrix.

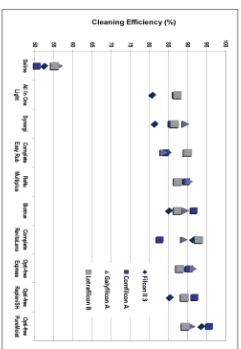


Figure 1 Relative lipid cleaning efficiency for a range of materials and MPS

The second question to ask relates to the critical micelle concentration. Simple surfactants are tadpole-like molecules which have a hydrophobic chain of around 10-20 carbon atoms with a polar head group to provide water solubility. An example is stearic acid in the form of its sodium salt. The hydrophobic tail tries to escape from water and packs into the surface – in so doing it changes the surface characteristics of the aqueous surfactant solution thereby reducing the surface tension. Once the surface becomes packed with surfactant molecules the hydrophobic tails of the surfactant “tadpoles” try to avoid contact with the water molecules by clustering together into spherical micelles.

The concentration at which the surface becomes fully packed and the excess surfactant begins to form micelles is called the **CRITICAL MICELLE CONCENTRATION** or CMC. The sharp change in concentration is illustrated in the inset graph in Figure 3.

There are two complicating factors that affect MPS behaviour. The first is that surfactants used in MPS behave in a more complicated way because they are very large molecules (typically Pluronics and Tetricons) which are used to minimise disruption of the ocular surface. The centropiece cartoon illustrates the relative size of a typical Pluronic in comparison to a conventional surfactant molecule. The second complication is that cleaning processes involve surface agitation which we can replicate by agitating the solution when we measure surface tension and CMC. This technique is known as **DYNAMIC SURFACE TENSION (DST)**.

Surfactants are recognised to play a vital role in multipurpose care solutions. Over the last two decades a range of surfactants varying in size and structure has been used in commercial products. Available MPS formulations contain different surfactants, different quantities and also mixtures of surfactants. Although requirements for antimicrobial efficacy are closely defined there are no parallel criteria for physicochemical performance. Requirements for approval that relate to surfactant performance vary between regulatory authorities but these data are not available to practitioners. Critical micelle concentration (CMC) appears to be one criterion used by the FDA but this aspect of surfactant behaviour within the class of surfactant used in MPS is quite different from that encountered in the simpler surfactants (such as washing-up liquid) that were used to define the meaning of a CMC. This poster illustrates the relationship of this, and other in vitro measures to one clinically relevant aspect of behaviour – cleaning ability. Cleaning ability is only one aspect of MPS behaviour that affects lens performance. Others include lens wettability, surfactant persistence and tear film stability.

We can use both static surface tension measurements and dynamic surface tension measurements to observe the critical micelle concentrations in both MPS and their constituent surfactants, and determine whether the CMC of MPS gives a useful indication of their cleaning capability. Figure 2 shows the change in static surface tension of a range of MPS at various dilutions expressed in terms of fractional concentration of the MPS. It is clear from Figure 2 that the surface tension-concentration plot of the MPS is very much less distinct than that of the simple surfactant shown in the inset of Figure 3.

Figure 3 also shows that the CMC of the most effective MPS in terms of lipid removal is not characterised by a low and distinct CMC even when many experimental points are collected using DST.

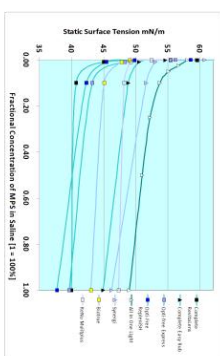


Figure 2 Static surface tension of various MPS as a function of dilution

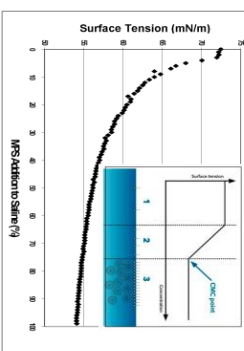


Figure 3 Dynamic surface tension vs. concentration of Optifree PureMoist

Precise CMC determination in block copolymer systems is difficult partly because these copolymers are frequently heterogeneous with respect to both composition and molecular weight. CMC values are not good single parameter predictors of MPS cleaning capability but surface tension (particularly dynamic) gives a strong indication of surfactant behaviour. Chosen of individual surfactant structure and concentration reflects a balance of cleaning performance with other factors that affect perceived ocular response to the MPS.

Purpose

Although CMC clearly shows no direct correlation with cleaning efficiency as transitions are indistinct and do not show clear variation, inspection of Figure 1 shows that surface tensions themselves do vary significantly. Figure 5 collects static surface tension behaviour for a range of MPS which show some variation without great discrimination. Figure 6 shows a similar range of MPS studied with dynamic surface tension – here the variation with agitation shows good general correlation with cleaning performance.

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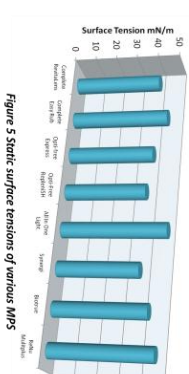


Figure 5 Static surface tension of various MPS

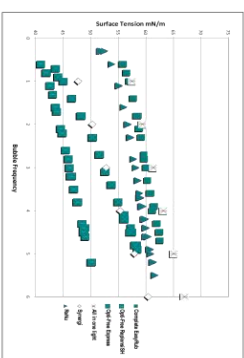


Figure 6 Dynamic surface tension of various MPS as a function of agitation

These and other results show that cleaning capability and persistence increased (but not proportionately) with surfactant molecular weight: e.g. Tetricons 1304 > 904; Pluronic 127 > 87. Significantly, MPS surfactant concentrations do not always reflect the CMC of the parent surfactant but is also influenced by the individual components included in the solution compositions. Cleaning capability of MPS is not simply related to surfactant CMC (critical micelle concentration), but dynamic surface tension measurements provide useful predictive information.

Conclusions

Precise CMC determination in block copolymer systems is difficult partly because these copolymers are frequently heterogeneous with respect to both composition and molecular weight. CMC values are not good single parameter predictors of MPS cleaning capability but surface tension (particularly dynamic) gives a strong indication of surfactant behaviour. Chosen of individual surfactant structure and concentration reflects a balance of cleaning performance with other factors that affect perceived ocular response to the MPS.

References: 1. Ross, G.M. Franklin, V.J. Tighe, B.J. Link Between Cleaning Efficacy & Physical Properties of Multipurpose Solutions: Contact Lens and Anterior Eye, Volume 34, 51, 2011, Pages 329-3; Ross, G.M. & Tighe, B.J. Physicochemical Assessment of Surfactant & MPS Formulations: Tools & Techniques Poster presented at Symposium on the Materials Science & Chemistry of Contact Lenses New Orleans 2011, 3. Tighe, B.J. & Tighe, B.J. In vitro Assessment of Cleaning Effectiveness of Care Solutions: Contact Lenses Poster presented at BCLA Conference 2010, 7. Shaw, D.J. Introduction to Colloid & Surface Chemistry Third Edition 1980, 3. Carnell, S.M., Ross, G.M. & Tighe, B.J. Pluronics, Tetricons & Care Solutions: Does Size Matter? Poster presented at BCLA Conference 2010, 6. Broadhead, M.J. Hsiao, A. & Tighe, B.J. Modelling the Impact of Tear Film on Lens Surface & Reverse Osmosis: Schematics Poster presented at BCLA Conference 2010

Plurionics, Tetronics and Care Solutions: Does Size Matter?

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Fig 1

Fig 2

Plurionics® and Tetronics® (Poloxamers and Poloxamines) are high molecular weight block copolymers. Their large size allows them to interact with contact lenses without being absorbed into the lens material. They have hydrophilic (water loving) ends and hydrophobic (water hating) centres (see Figs 1&2). This means they behave as surfactants with the hydrophobe being attracted to surfaces. They have low toxicity and do not interact aggressively with the cornea, which allows them to be introduced directly into the eye. They differ in molecular size and hydrophilicity and these properties are indicated by their individual descriptor. For example F127, the first letter indicates the physical state of the starting polymer – 'F' for flake. The last digit indicates the weight % of the hydrophilic polymer (poly ethylene oxide) thus: 7x 10 = 70wt% hydrophilic. The first number indicates the molecular weight of the hydrophobic segment of the polymer (poly propylene oxide) thus: 12 x 300 = 3600g/mol. The 'Tetronic®' descriptor includes an additional zero which should be ignored.

Name	Hydrophobe size x 300g/mol	Hydrophilic wt % x 10
904	9	0.4
1107	11	0.7
1304	13	0.4
1307	13	0.7
F127	12	7

Methods

Commercially available medium water content silicone hydrogel contact lenses were soaked over night (approximately 12 hrs) in 1% solutions of Tetronic® 904, 1107, 1304 and 1307. These Tetronics® were chosen as they vary in size and hydrophobicity. Subsequently the lenses were soaked in distilled water repeatedly (see diagram below) for different times: 1 Second (repeated agitation), 4 minutes and 56 minutes)



The experiments were carried out using methodology developed in the Biomaterials Research Unit. The surface tension of the resulting solutions was then measured using the Du Noy Ring Method. Friction experiments were also carried out on the unwashed soaked lenses, using saline as the lubricant.

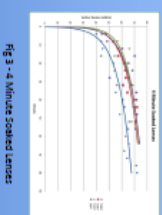
E-mail: Contact: carnelism@aston.ac.uk

Cleaning → **Comfort**

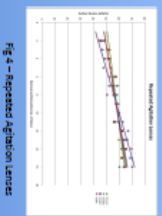
Compatibility

Introduction

In recent years an increasing number of contact lens cleaning solutions have included a range of surfactants called Plurionics® and Tetronics®. The addition of surfactants to care solutions was initially simply designed to remove debris and deposits from the lens. This poster shows that after overnight soaking Plurionics® and Tetronics® in contact lens care solutions remain attached to the lens surface. The surfactant remaining on the contact lens, leads to increased wettability of the lens and that is linked to improved comfort during contact lens wear.



Surfactant	Time (mins)
T904	36
T1107	36
T1304	76
T1307	44



Results and Discussion

From the Graphs shown in Fig 3 and 4 the effect of soaking and agitation on persistence is seen. Fig 3 shows the marked differences in the persistence curves, particularly in the early stages, together with longer term differences depending on the Tetronics® used. It is obvious from the graph the T1304 is most persistent. The other Tetronics® follow a similar pattern to each other. The time by which the soaking solution reached a water like surface tension (72.8 mN/m) is shown in Table 1. The order of most persistence is T1304>T1307>T1107>T904. This indicates that the size of the molecule and its hydrophobicity are factors in regards to persistence. Fig 4 shows that more marked agitation produces a more linear decay in persistence with less distinction between the Tetronics®. The order of persistence is again T1304>T1307>T1107>T904 showing that the importance of molecule size is maintained as agitation conditions change.

Fig 5 illustrates the persistence of Tetronic® when the lenses are left to soak with no agitation. The change in surface tension between 56 and 60 minutes indicates that T1107 shows the greatest loss. The order of persistence here is T1304>T904>T1307>T1107. This suggests that hydrophobicity assumes greater importance in non-agitated systems. Fig 6 shows the difference in surfactant loss between 4 minute agitation and repeated agitation.

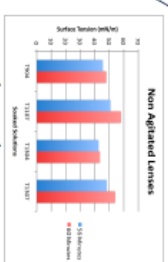


Fig 5 - Non Agitated Lenses

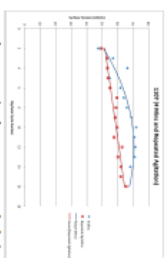


Fig 6 - T1107 (4 min and repeated agitation)

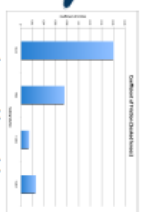


Fig 7 - Coefficient of friction

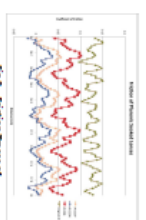


Fig 8 - Friction Traces of Soaked lenses

Fig 7 shows how the lubricity (coefficient of friction) of the lens is affected by Tetronic® soaking, expressed as an average value taken over 10 runs. Fig 8 shows the friction traces over a section of one run – illustrating Classic 'stick-slip' behaviour. Figs 7 & 8 are consistent with the persistence graphs (Fig 3 & 4) showing T1304 surfaces as the most lubricious (lower friction) followed by T1307 and T904.

Conclusion

- Soaking lenses in Pluronic® and Tetronic® solutions leads to adsorption which advantageously affords properties such as wettability and lubricity.
- Because surfactant on the lens improves wettability and lubricity whereas release into the tear film destabilises the lipid layer prolonged persistence is desirable.
- The persistence of the adsorbed layer and the kinetic form of the desorption process are both markedly affected by agitation conditions.
- Plurionics® and Tetronics® do not perform identically their persistence at the lens surface is influenced by both size and hydrophobicity – size matters!



Dehydration at the lens surface: surface energy and surfactant persistence



Introduction

Dehydrated Surface Analysis

Contact lens surface analysis is often made using a sessile drop water contact angle on a fully hydrated lens. This produces very low contact angles and shows minimal differences between lens materials. When the lens is dehydrated fully and the sessile drop water contact angle is measured the angles are much larger and show greater differences between the materials. The fully hydrated and dehydrated lenses show the extreme conditions a lens material could be exposed to. Being aware of the material behaviour in these conditions gives an insight into how the lenses will behave in less extreme conditions. During lens wear the material will lose hydration over time but will not become completely dehydrated.

Surface Free Energy (V)

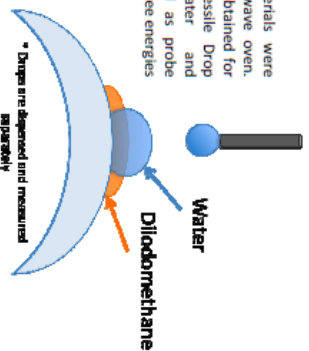
Using water (highly polar) to create a contact angle measures the wettability of the lens. By using an additional probe liquid such as diiodomethane (non-polar/dispersive) the surface free energy of the material can be calculated. All materials have surface free energy. This can be split into two components, dispersive (V_d) and polar (V_p). V_p refers to intermolecular forces which occur in every material and V_d refers to forces caused by permanent dipoles. Surface free energy allows for characterisation of the dehydrated material and provides an additional approach to surface analysis.

Surfactant Persistence

Water soluble species with hydrophobic domains (such as surfactants) interact directly with the hydrophobic domains in the lens polymer. When the lens is fully hydrated the hydrophobic domains are hidden and the surfactant will have limited interaction with the hydrophobic domains. However, reducing the lens hydration exposes more hydrophobic domains at the lens surface allowing for more surfactant molecules to attach to the lens. It has been shown that surfactants do persist for a short time on the lens surface when the material is fully hydrated, but can this time be increased by dehydrating the lens prior to surfactant exposure?

Dehydrated Sessile Drop

Several contact lens materials were dehydrated using a microwave oven. Contact angles were then obtained for all materials using the Sessile Drop method. HPLC Water and Diiodomethane were used as probe liquids to allow for surface free energies to be calculated.



Methods

The Owens-Wendt Model (below) calculates both the dispersive and polar components of a material.

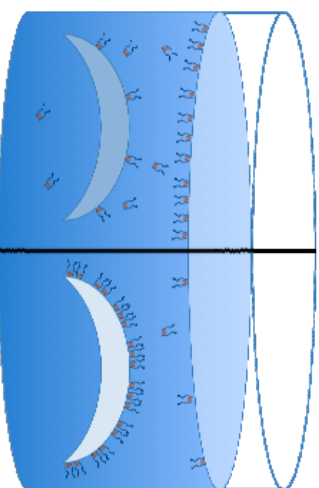
$$1 + \cos\theta = 2\sqrt{\gamma_d} \left(\frac{\gamma_d}{\gamma_{lv}} \right) + 2\sqrt{\gamma_p} \left(\frac{\gamma_p}{\gamma_{lv}} \right)$$

The polar fraction (V_p) value $\left(V_p = \frac{\gamma_p}{\gamma_d + \gamma_p} \right)$ was used as an indication of material wettability.

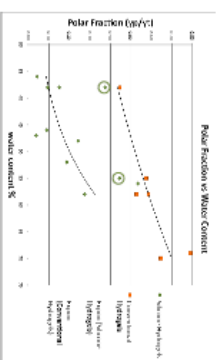
Dehydrated Lens Modification

Surfactants have been shown to increase the wettability of a contact lens surface and are often used to do just that in commercial lenses.

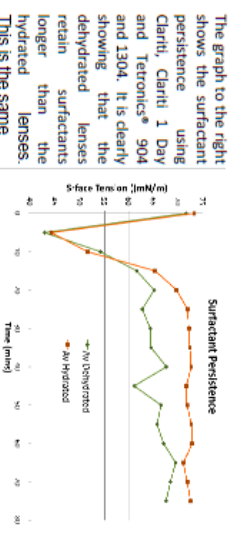
Surfactants have hydrophobic and hydrophilic poles, the hydrophobic pole is attracted to the hydrophobic domains on contact lens surface. This exposes the wettable hydrophilic pole. Conventionally contact lenses are introduced to surfactants when the lenses are in a hydrated form. Hydrated lenses have few hydrophobic domains at the surface. If a dehydrated lens is exposed to the very same surfactant solution there is an increase in hydrophobic area for the surfactant to attach to. (see below)



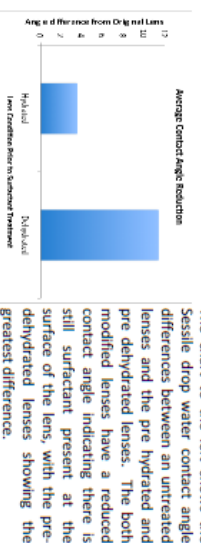
Results



The graph to the left shows that when lenses are dehydrated, a higher initial water content leads to a higher polar fraction (V_p). Conventional lenses have a higher V_p than silicone lenses. Unusually, plasma coated lenses show



for both lenses and both surfactants.



Conclusions

Surface Free Energy is a useful tool in characterising contact lenses and predicting behaviour. Dehydrating the lens materials allows for extreme conditions to be measured. Silicone Hydrogels have a different polar fraction trend to conventional hydrogels and plasma coated silicone hydrogels behave more like conventional hydrogels.

After dehydration the lenses with higher hydrated water content show a higher PF. Higher hydrated materials have a higher affinity for water regardless of the current hydration.

Dehydrating the lens prior to surfactant soaking increases the persistence of the surfactant at the surface.

1. 2010 BCA conference abstracts, Contact Lens and Anterior Eye, 2010, Vol 33, 256-300

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The use of silicone-based materials in the daily disposable regime has been growing steadily. The enhanced Dk of Silicone Hydrogels (SH) offers advantage over conventional hydrogel (CH) materials. However SH lenses are more complex to manufacture than CH and the need to increase scale and reduce costs (relative to lenses used for weekly – monthly wear modalities) presents particular challenges. This makes a comparison of what can presently be achieved with SH and CH lenses particularly interesting and clinically relevant. The surface characteristics properties are known to be influential in wearer comfort. Here we analyse surface properties of a range of materials (Dailies Basic, Dailies Aqua Comfort Plus, Dailies All Day Comfort, neiflicon A, Dailies Total1 delectifcon, Acuvue 1 Day, Acuvue 1 Day Moist etafilcon A, Acuvue TruEye natrifilcon A and Clariti 1Day filcon 3 II), using modified nano scratch tester (Friction), sessile drop (Surface Free Energy) and Wilhelmy Dynamic Contact Angle (DCA).

Friction

Lenses were removed from the packing solution, blotted, and analysed using a protocol similar to Ross et al ¹. Lenses were tested under eye-lid load, with Hypo Tears® as the lubricant and Melinex® the substrate. The coefficient of friction (CoF) and Stick-slip factor (SSF) can be extracted from the recorded data. The mean CoF and SSF is shown in the table below.

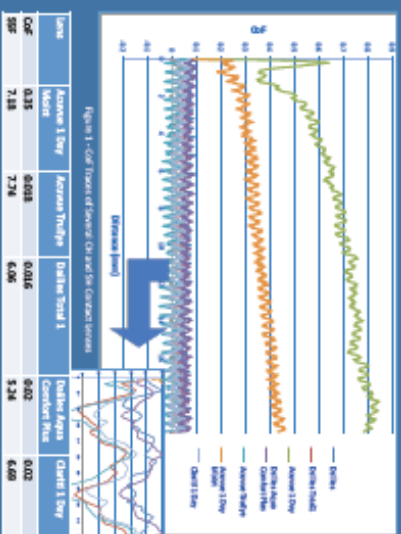


Figure 1 - CoF (N) versus Time (s) for various lens materials

The order of CoF for CH materials was Acuvue 1 Day > Acuvue 1 Day Moist > Focus Dailies = Focus Dailies Aqua Comfort Plus. The incorporation of LACRION® technology significantly reduces the CoF of Acuvue 1 Day base material. The low modulus of Acuvue 1 Day influences the CoF. Softer materials such as Acuvue 1 Day tend to have higher CoF.

The SH lenses all have lower CoF than CH, and under eyelid load were ordered Clariti 1 day > Dailies Total1 > Acuvue TruEye. SSF was ordered Dailies Total1 < Clariti 1 Day < Acuvue TruEye.

Surface Free Energy (SFE)

(Dehydrated surface)

Lenses were removed from the packing solution, briefly washed with PBS, blotted and dehydrated for 5 minutes in a microwave. The sessile drop method² was then used to measure (water and diiodomethane) contact angles of the dehydrated surface. Polar and dispersive surface energies were calculated using the Owens-Wendt equation ².

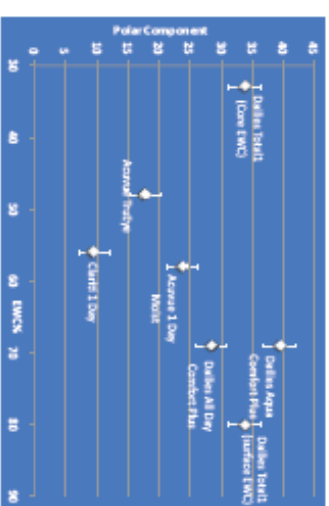


Figure 2 - Polar Component and Equilibrium water content of new CH and SH Contact Lenses

-A plot of equilibrium water content (EWC) vs the polar component of SFE of the dehydrated lenses (Figure 2) separates the CH and SH materials. This is expected due to the hydrophobicity of the silicone-based SH material constituents.

-The polar component of the dehydrated lenses of a given water content indicates the extent to which hydrophilic groups (e.g. silicone) groups mask (at the surface) the hydrophobic groups that drive water uptake. Processing aids can also influence values for DD SHs.

DCA

Lenses were removed from the packing solution, and briefly washed in PBS. The lenses were analysed using a dipping rate of 0.2mm/s in air³. Advancing and receding contact angles were then calculated. The surface tension of the probe solution was measured before and after the runs.

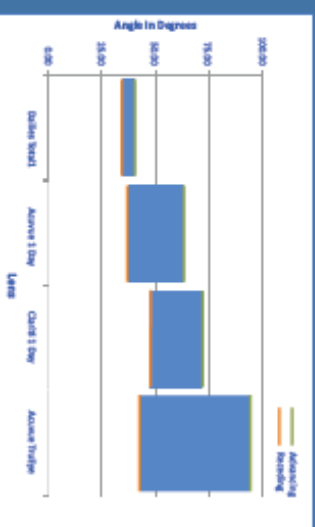


Figure 3 - Advancing and Receding Angles of Dehydrated lenses and Acuvue 1 Day

-The advancing and receding contact angles are shown on Figure 3. Contact angle hysteresis is indicated by the blue bar on the figure.

-A low advancing angle and reduced hysteresis is a common goal in contact lens materials design.

-The order of advancing contact angles is Total1 < Clariti < TruEye.

-Uncoated Acuvue TruEye has the highest advancing angle and the largest hysteresis, whilst Dailies Total1 with a high (>70%) water content coating shows the lowest advancing angle and the smallest hysteresis. This lens shows hydrogel-like characteristics in SFE and DCA, indicating that the silicone surface is effectively masked by a substantial hydrogel coating.

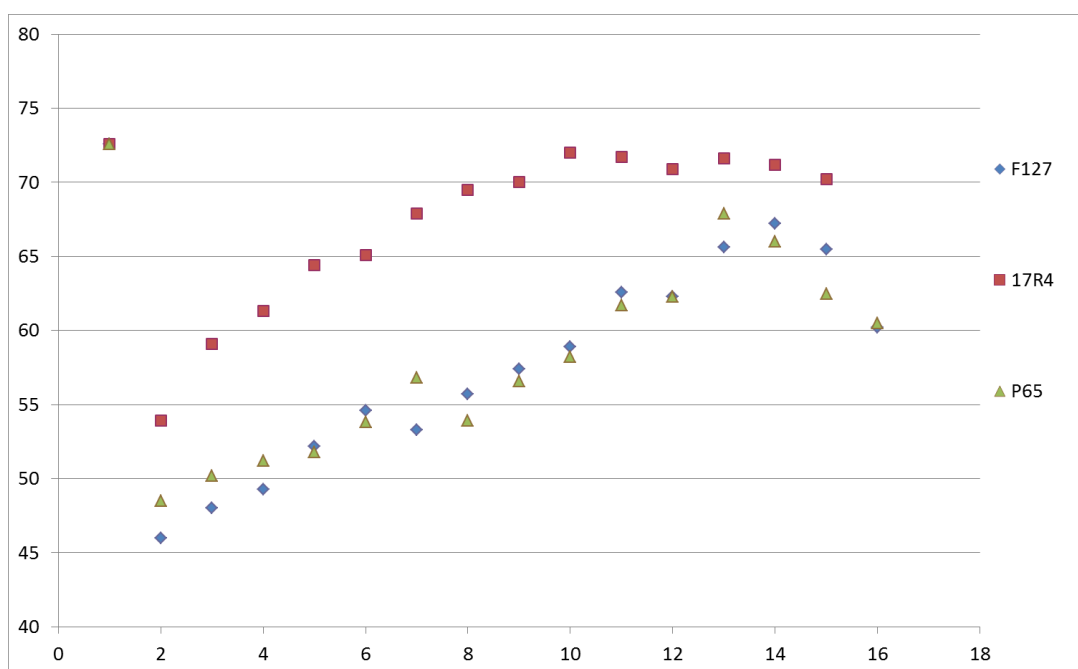
Conclusion

The three techniques highlight different trends between uncoated SH and CH materials. Interestingly, CoF of Dailies Total1 is not very different from Acuvue TruEye or the other Dailies lenses and all of these use different techniques to lubricate the surface⁴. The SFE method showed separate trends for SH and CH, but both demonstrate that an increase in the hydrophilic groups that drive EWC will increase the polar component of dehydrated lens surfaces. DCA results suggest that Dailies Total1 has a sufficiently thick hydrogel layer to mask typical SH behaviour. All the lenses in this poster have shown good clinical performance. Based on the surface techniques used here however, Dailies Total1 appears to behave more like a CH, and is the most wettable SH (for this selection of materials).

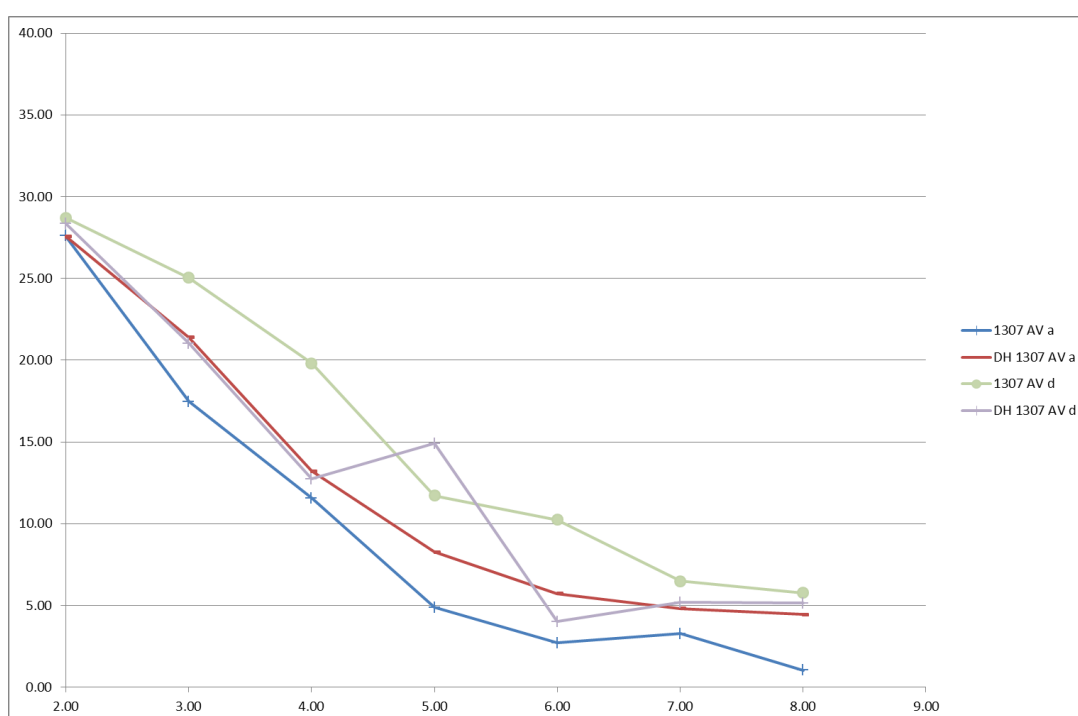
S M Cornell would like to thank EPSRC for Studentship funding and Sanofi Pharmaceuticals limited for CoSE support.

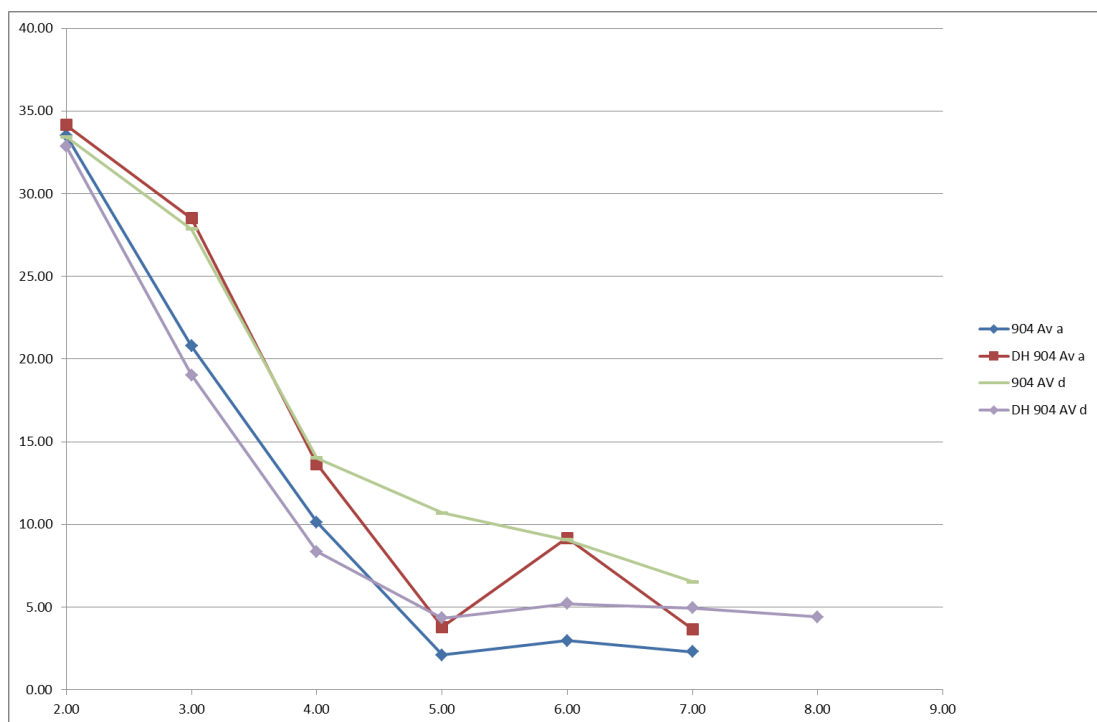
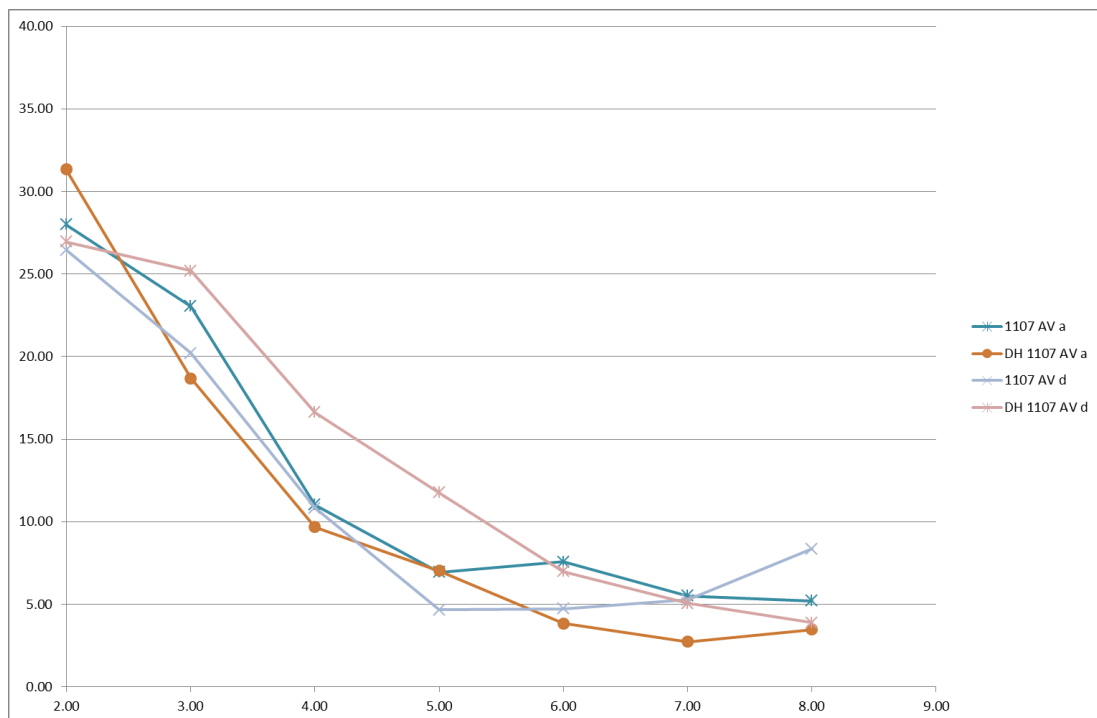
¹ Ross, S. J. et al. (2005) 'The effect of lens material and design on the performance of daily disposable contact lenses', *Optometry*, 76, 1-10.
² Owens, K. J. et al. (1981) 'A method for determining the surface free energy of polymers', *Journal of Polymer Science: Part A: Polymer Chemistry*, 19, 1701-1713.
³ Davies, J. et al. (2005) 'The effect of lens material and design on the performance of daily disposable contact lenses', *Optometry*, 76, 1-10.

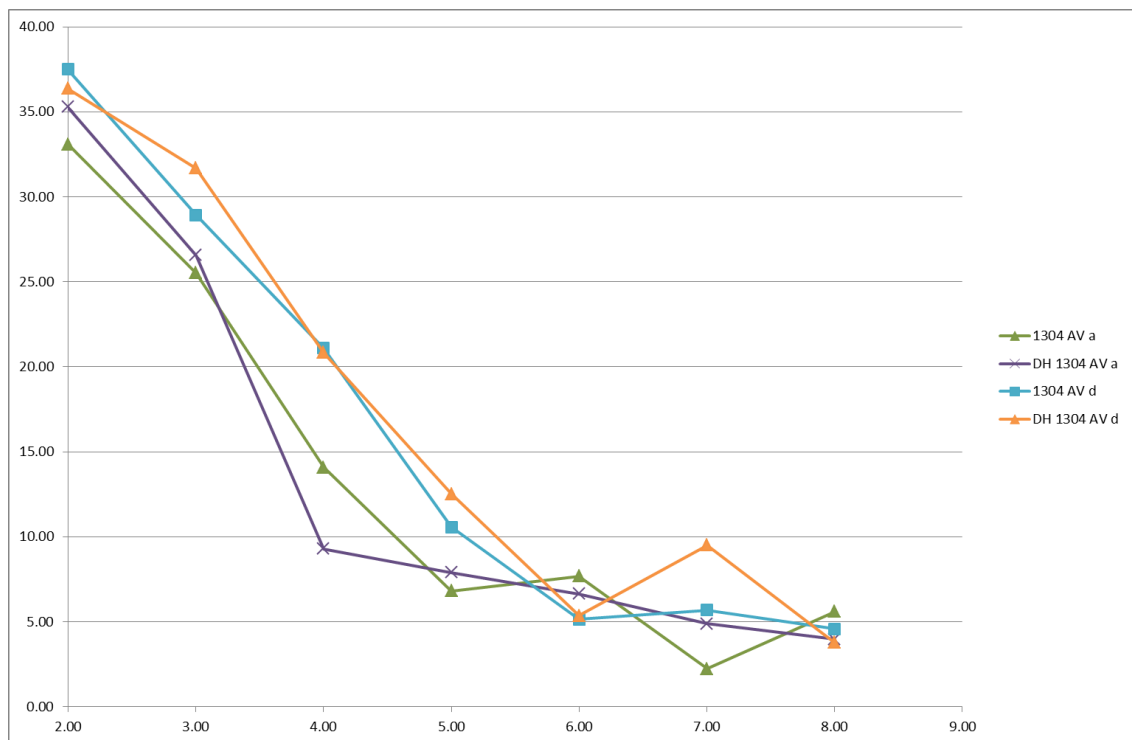
9.2.Elution Model A data



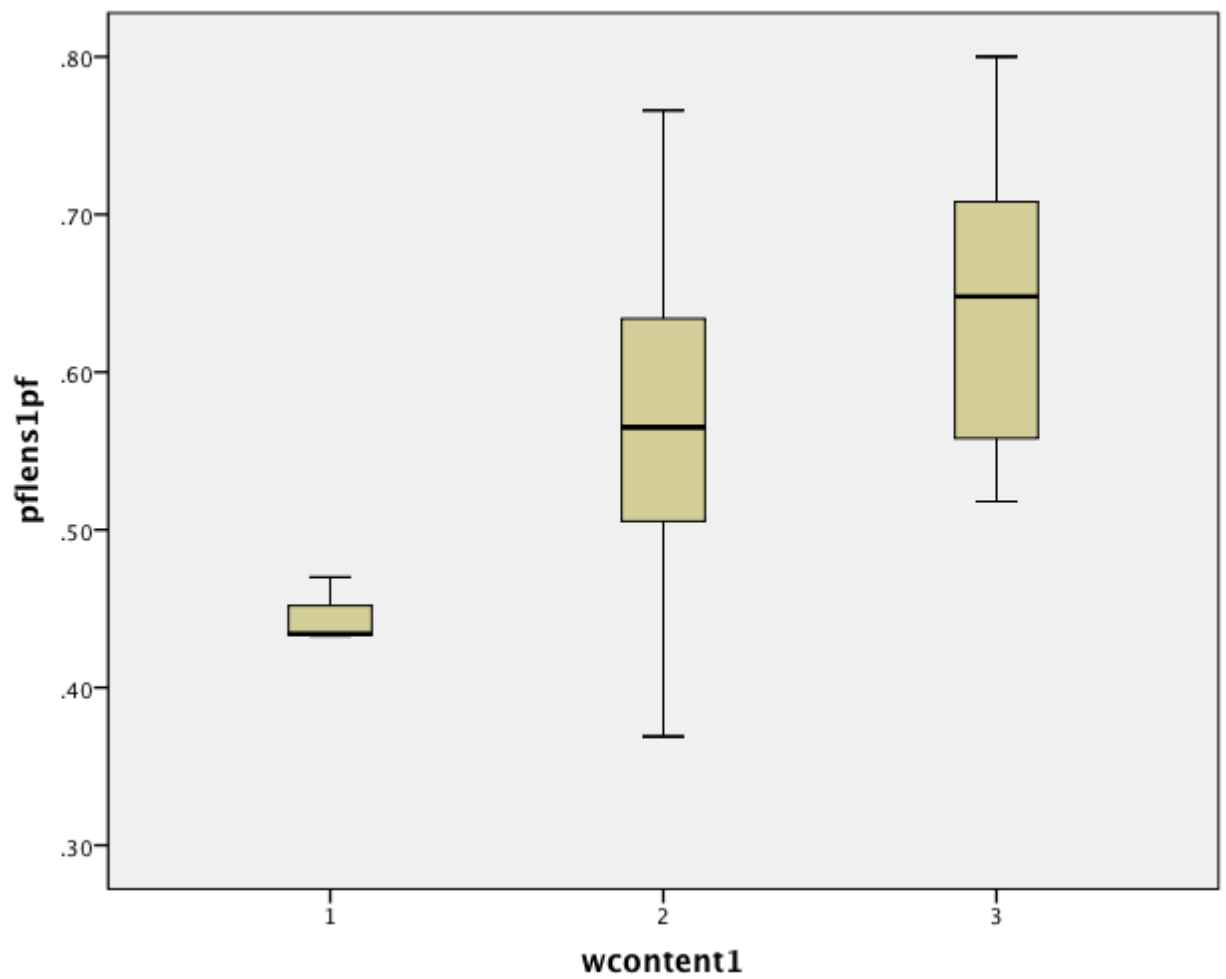
9.3.Elution Model B data







9.4.Twoway ANOVA for Figure 3.3.3



ANOVA

pflens1pf

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.104	2	.052	5.596	.010
Within Groups	.241	26	.009		
Total	.345	28			

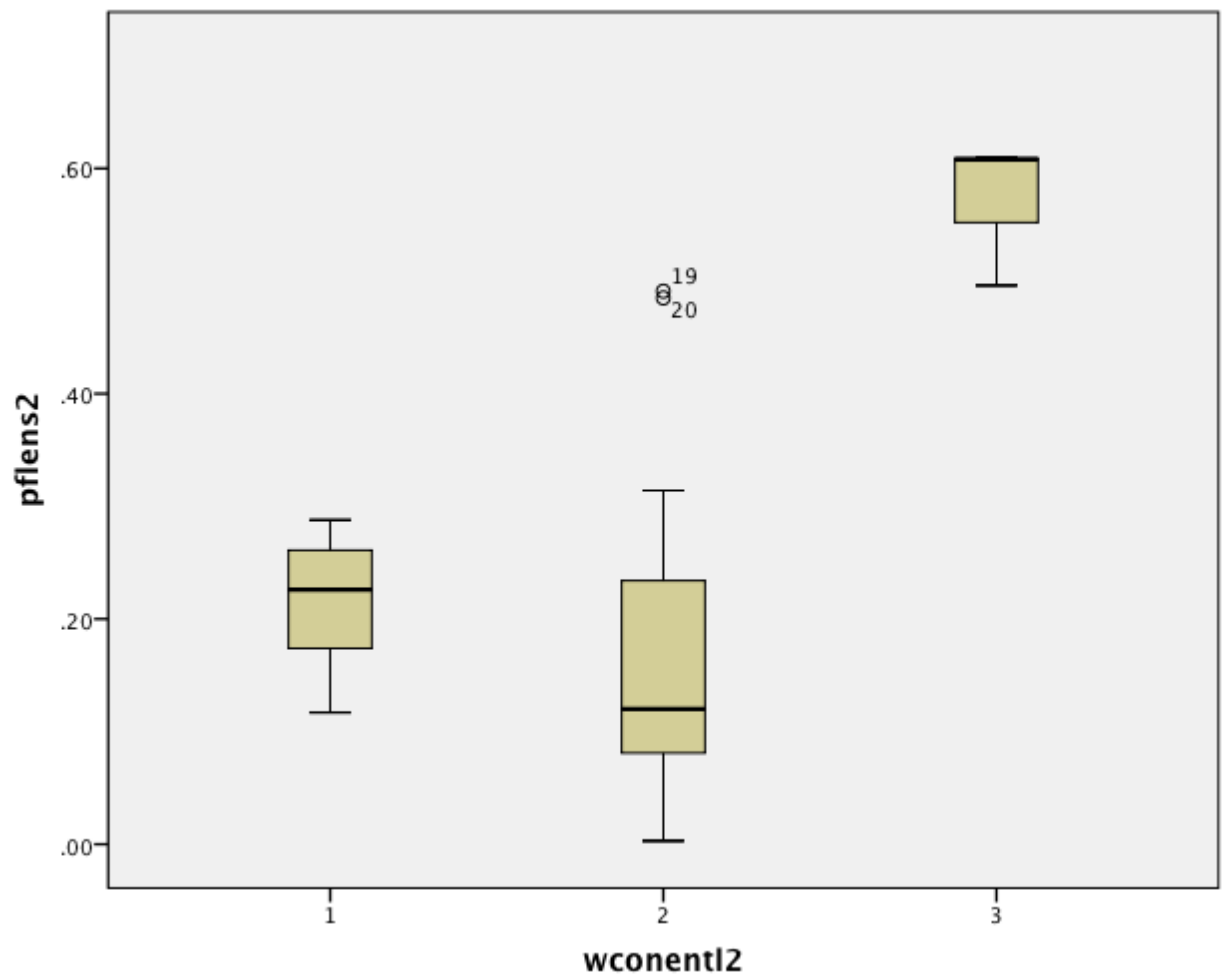
Multiple Comparisons

Dependent Variable: pflens1pf

LSD

(I) wcontent1	(J) wcontent1	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	-.11633	.06093	.067	-.2416	.0089
	3	-.19824*	.06275	.004	-.3272	-.0693
2	1	.11633	.06093	.067	-.0089	.2416
	3	-.08191*	.03824	.042	-.1605	-.0033
3	1	.19824*	.06275	.004	.0693	.3272
	2	.08191*	.03824	.042	.0033	.1605

*. The mean difference is significant at the 0.05 level.



ANOVA

pflens2

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.419	2	.209	12.943	.000
Within Groups	.372	23	.016		
Total	.791	25			

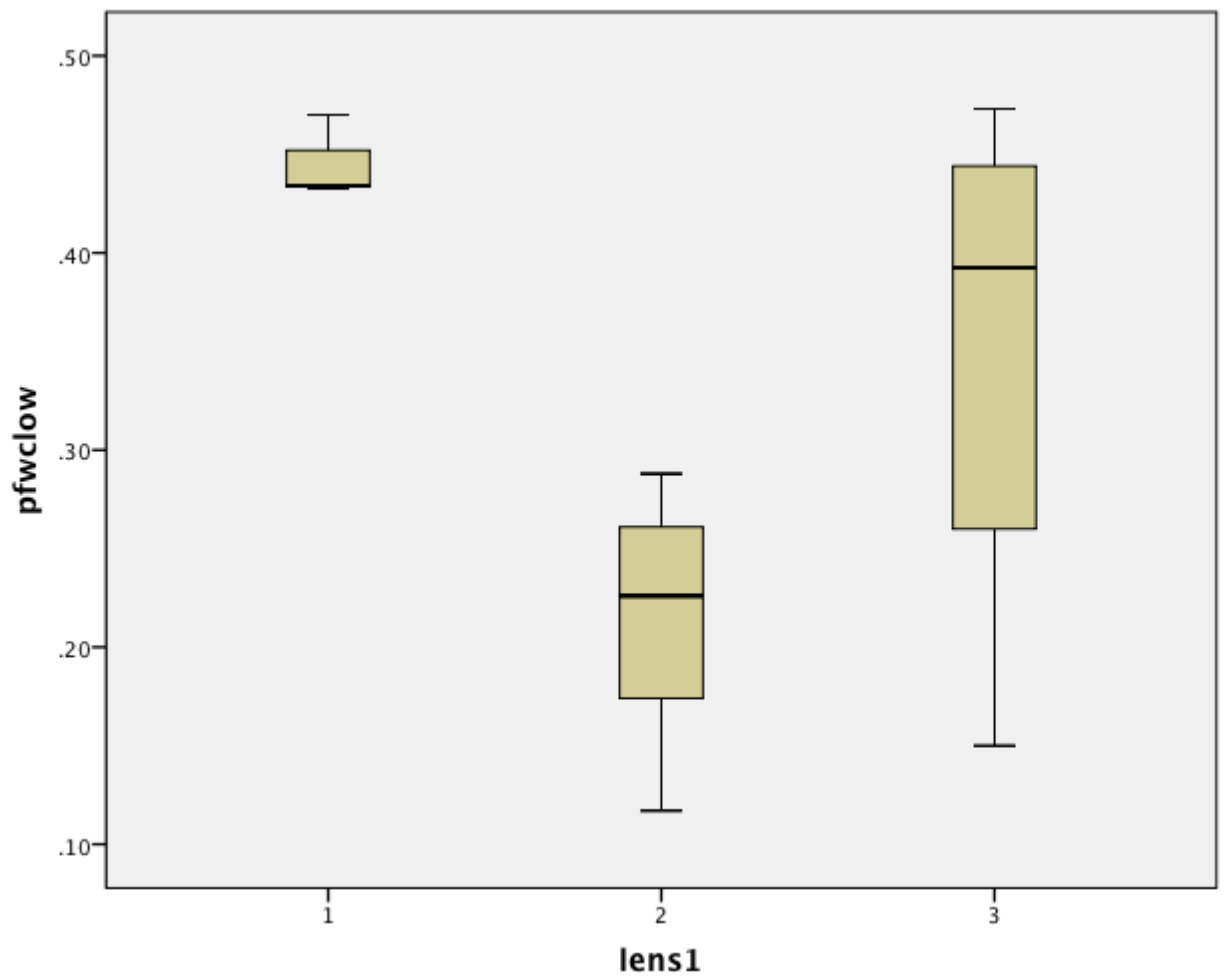
Multiple Comparisons

Dependent Variable: pflens2

LSD

(I) wcontentl2 (J) wcontentl2		Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	.04520	.06431	.489	-.0878	.1782
	3	-.35813 [*]	.09290	.001	-.5503	-.1659
2	1	-.04520	.06431	.489	-.1782	.0878
	3	-.40333 [*]	.07933	.000	-.5674	-.2392
3	1	.35813 [*]	.09290	.001	.1659	.5503
	2	.40333 [*]	.07933	.000	.2392	.5674

*. The mean difference is significant at the 0.05 level.



ANOVA

pfwclow

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.108	2	.054	6.141	.021
Within Groups	.079	9	.009		
Total	.188	11			

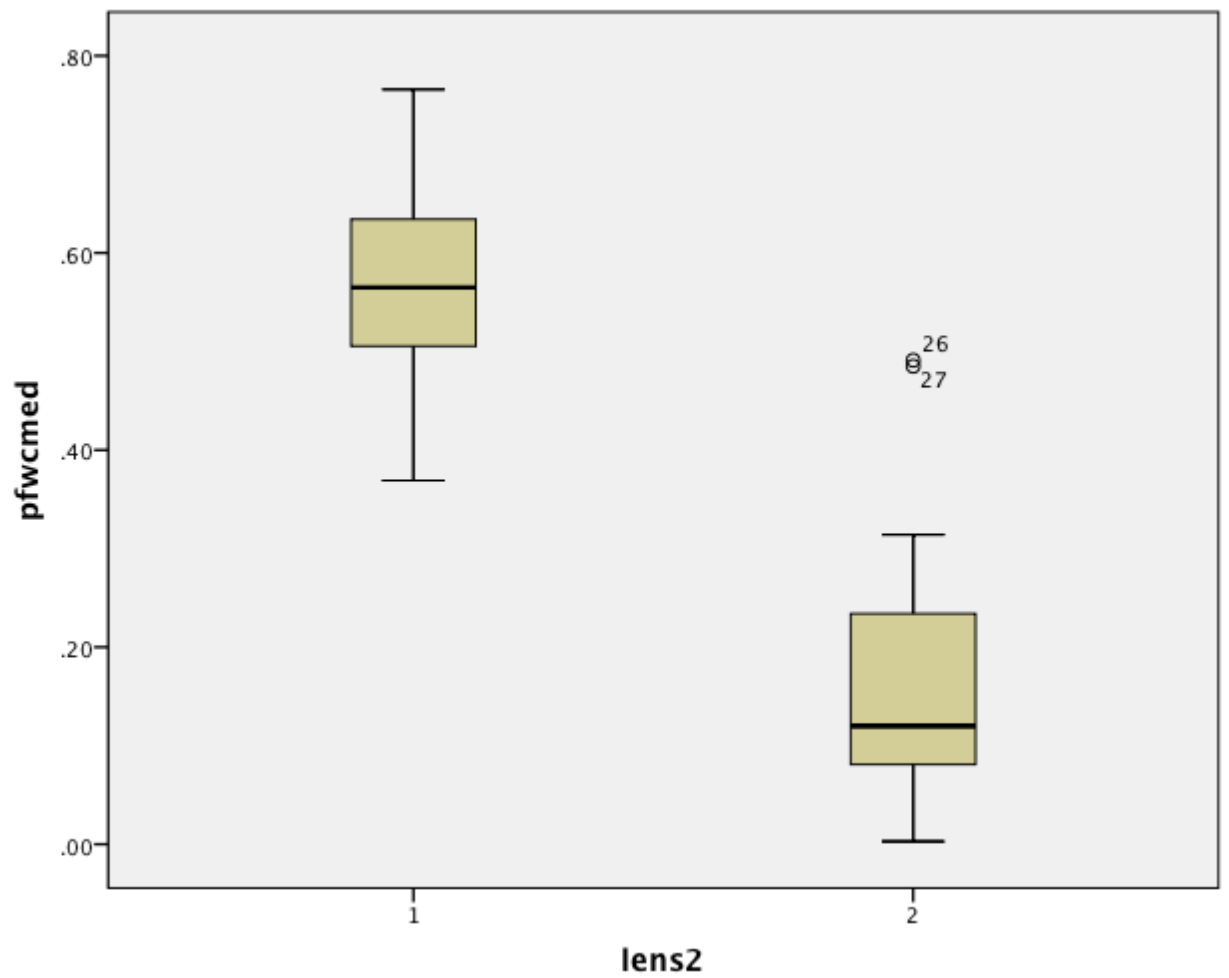
Multiple Comparisons

Dependent Variable: pfwclow

LSD

(I)	(J)	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	.23247*	.06862	.008	.0772	.3877
	3	.09367	.07177	.224	-.0687	.2560
2	1	-.23247*	.06862	.008	-.3877	-.0772
	3	-.13880	.06303	.055	-.2814	.0038
3	1	-.09367	.07177	.224	-.2560	.0687
	2	.13880	.06303	.055	-.0038	.2814

*. The mean difference is significant at the 0.05 level.



Group Statistics

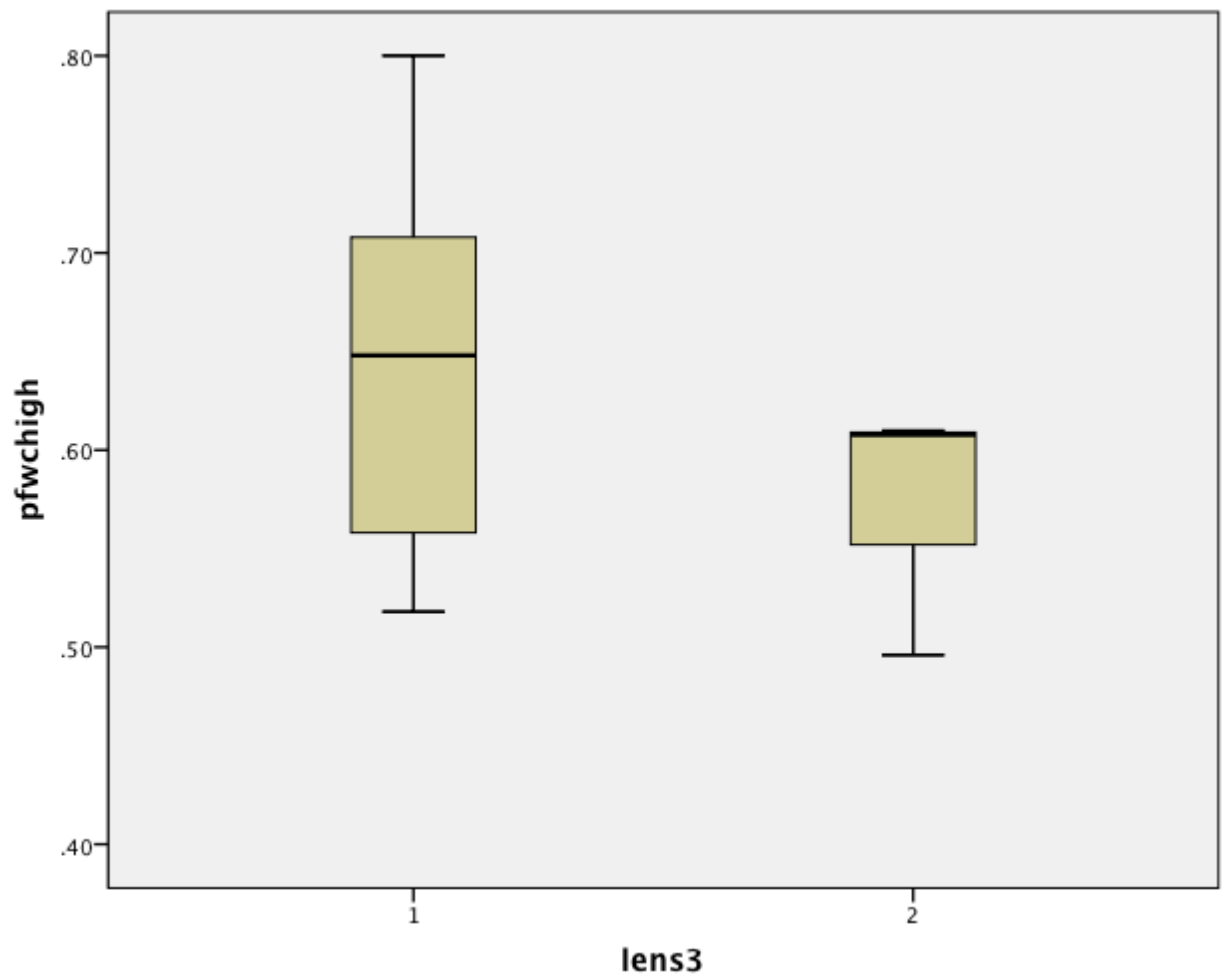
	lens2	N	Mean	Std. Deviation	Std. Error Mean
pfwcmed	1	15	.5620	.10222	.02639
	2	18	.1680	.14243	.03357

Group Statistics

	lens2	N	Mean	Std. Deviation	Std. Error Mean
pfwcmed	1	15	.5620	.10222	.02639
	2	18	.1680	.14243	.03357

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
pfwcmed	Equal variances assumed	1.415	.243	8.953	31	.000	.39400	.04401	.30425	.48375
	Equal variances not assumed			9.226	30.405	.000	.39400	.04270	.30683	.48117



Group Statistics

	lens3	N	Mean	Std. Deviation	Std. Error Mean
pfwchhigh	1	11	.6439	.09704	.02926
	2	3	.5713	.06525	.03767

Group Statistics

	lens3	N	Mean	Std. Deviation	Std. Error Mean
pfwchigh	1	11	.6439	.09704	.02926
	2	3	.5713	.06525	.03767

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
pfwchigh	Equal variances assumed	.632	.442	1.205	12	.252	.07258	.06025	-.05870	.20385
	Equal variances not assumed			1.522	4.792	.191	.07258	.04770	-.05166	.19681

9.5.Other Statistical Data

Correlations

		modulus	stickslip
modulus	Pearson Correlation	1	-.505
	Sig. (2-tailed)		.166
	N	9	9
stickslip	Pearson Correlation	-.505	1
	Sig. (2-tailed)	.166	
	N	9	9

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